

Setback for Mr Micawber

THE settlement of the British miners' strike this week is not merely a short-term economic disaster but a sign that the British government, whatever its inclinations, must sit down and solemnly attempt to work out a policy for the use of different kinds of fuel between now and the end of the 1980s. The events of the past few weeks have shown quite plainly that the hand-to-mouth expedients which have been used to rig the market in fuel do not add up to a policy but that, if anything, they are a negation of a fuel policy. To the extent that the British case resembles that of many other countries in Western Europe, it may be of more than merely local interest. To the extent that many of the steps which now need to be taken require European rather than British arrangements, the problems which the British government must solve will compel it towards economic innovation.

The recommendations of the court of inquiry under Lord Wilberforce which provided the basis for settlement between the National Coal Board and the miners are alarming for two different kinds of reasons. In the first place, whatever arguments the Wilberforce committee and the government have put forward to suggest that miners have a special claim for an increase of weekly earnings which works out at an average of 20 per cent, it is hard to see that it will now be possible to restrict the claims of other groups of workers to the seven or eight per cent on which the government appears to have pinned its hopes for a modicum of economic stability. Since, even before the industrial disruption caused by the lack of coal at power stations, industrial production in Britain this year was estimated to grow by merely four per cent, even this modest target presupposed a measure of wage inflation. The chances now are that the present year will see an inflationary pressure which exceeds the three or four per cent to which the government appears to have been reconciled. In other words, historians will be required to count 1972 among the years in which successive British governments have failed to regulate the economy in such a way that extra earnings are paid for out of extra production. That, as it turns out, is a cause for anxiety which transcends the more technical question of how to make a rational fuel policy.

The Wilberforce report is also a disaster because of the support that it provides for a further distortion of the fuel economy. In the first place, the recommendations of the Wilberforce committee support the implicit understanding between the miners and the coal board that miners should be paid at the same rates, wherever they work in British collieries, even though some coal fields are much more productive and profitable than others. Although this understanding has helped to reduce the incidence of local labour disputes in the past few years, it must seriously be asked whether it makes economic sense. In agreeing to the miners' argument that surface workers at British collieries deserve the largest increases in pay because many of them are underground workers "redeployed on surface work because their health has been

adversely affected by working conditions underground", the court of inquiry has also connived at the notion that the National Coal Board should in part substitute for a just policy on industrial insurance an understanding that disabled miners will be recompensed with job security. Worse still, in calculating the annual cost of the wage increases which it recommends, the Wilberforce inquiry has lent support to the common demand of the miners and the National Coal Board that there should be a further rearrangement of its capital structure which would have the effect of reducing the sums of money it must pay each year in servicing its accumulated debt to the British government. The argument here is painfully thin. The miners argue that there is no reason why the present economics of the British coal industry should be burdened by the cost of paying for collieries put out of action in the past decade and that it is unfair that the National Coal Board should aim to provide out of current income a surplus to cover accelerated depreciation of the capital assets embodied in collieries which may be closed in the years which lie ahead. In other words, what the miners and to some extent the coal board are saying is that they should not be held responsible for the costs of shutting down production facilities which are no longer needed. On no interpretation of the relationship between a government and a nationalized industry is such an assertion tenable. It amounts to saying that the profitable parts of the British coal industry should not be expected to shoulder the costs of bankruptcies elsewhere. Especially because the coal board has failed to live by the rule, hopefully prescribed for it in 1967 by the then Ministry of Power and by the legislation which permitted a capital reconstruction of the industry in the previous year, that depreciation on current assets should be calculated at replacement costs, there is only the thinnest case for the removal of the coal industry's burden of debt. It is in all the circumstances preferable that the government should now bite on the bullet and insist that the capital costs of mining coal in Britain, the cost of meeting the increase of wages now agreed (estimated to be £100 million a year) and the current deficit of the National Coal Board (another £100 million a year) should be met by a substantial increase of the price of coal.

But will this not mean a still faster decline of the coal industry? This is what both the miners and the National Coal Board fear and, fair play, the Wilberforce inquiry does point out that when the government agrees to shield some parts of the industry from the consequences of too rapid a decline, it should explicitly calculate what it is prepared to pay so as to provide employment for regions in Britain where rapid decline would mean unpalatable unemployment in mining communities which cannot easily adjust to change. The trouble, of course, is that governments are congenitally cowardly on issues like these. For one thing, there are problems, especially for Conservative governments, in acknowledging that unprofitable industries are kept going so as to provide jobs



for people who would otherwise be compelled to join the dole queues. For another, there is always the danger that accurate calculations will show that the costs of providing unprofitable jobs are absurdly high. Yet it is hard now to escape the need to carry out such calculations and to make them publicly available. To do less will in the long run be to do injustice to the miners.

But what will be the increase in the price of coal and what are the implications for the scale on which the industry operates in future? If it turns out to be necessary for the National Coal Board to increase its income by £150 million a year (which supposes that there will also be a substantial increase of productivity), then simple arithmetic suggests an increase of the price of coal at the pithead of roughly 20 per cent. Left to themselves, the principal customers for British coal would no doubt wish to use other fuels instead, and already the Central Electricity Generating Board, which uses 75 million tons of coal a year, is complaining that coal is too expensive. In the circumstances, it would probably be prudent not too fiercely to drive these customers away, which in turn implies that other customers will be expected to pay more. But it is only a few years before Britain will be required by the regulations of the European Communities to establish a free market for coal, which in turn implies that, by 1975, the 50 million tons of coal sold each year to the general run of industrial and domestic users will be seriously at risk. In other words, the government and the National Coal Board should be reconciled to a further reduction of the output from British mines in the next three years which may be as much as 30 or 40 million tons of coal a year. Certainly there is now no hope that the coal board's objective of stabilizing production at the present level of 150 million tons a year can be attained. It is in everybody's interest that this prospect should be acknowledged openly, and that an immediate start should be made on identifying the social problems thrown up by a contraction that will imply not much more than 100 million tons of coal a year by 1975.

Where will the extra energy come from? It is a great paradox that the British government, which used in the early 1960s to boast about its sponsorship of nuclear energy, should in the past decade have allowed the nuclear industry to languish. A part of the trouble has been economic, for in calculating the relative costs of nuclear energy and electricity produced from coal-fired power stations, no allowance has been made for the inevitability of disproportionate increases in the cost of coal which are unavoidable in a labour-intensive industry such as coalmining. But there have also been technical muddles which spring at least in part from chauvinism. The huge gas-cooled thermal reactors which formed the backbone of the first generation of British nuclear power stations, and which now have a maximum output of more than 3,000 megawatts, have been a moderate disappointment, chiefly because of the way in which unforeseen problems of corrosion within the reactors have restricted output, but even so, the cost of electricity from these stations is comparable with that from some of the coal-fired stations now in service. The second generation reactors, called the advanced gas-cooled reactors, have been a greater muddle, chiefly because of the muddles which there have been in building the first station of any size, the now notorious Dungeness B reactor. In retrospect, it is a great mistake that the Central Electricity Generat-

ing Board decided against building at least a few water-cooled reactors when it had the chance, in 1965. The immediate future appears to depend on helium-cooled gas reactors operating at temperatures up to 750 degrees centigrade, but here again the commissioning process appears to be too cautious. Is this not a point at which the government should urge the CEGB to be more adventurous? Would it not be possible to aim at the installation of 2,000 megawatts or more of high temperature gas-cooled reactors by 1976, and three times as much installed capacity by the end of the decade, which would imply that there would by 1980 be 10,000 megawatts of nuclear generating capacity in Britain, roughly one sixth of the total installed capacity of the generating board by that year? The trouble, with present arrangements, is that such a target will be reached only if the British government can bring itself to persuade the electricity authorities that such a target is necessary as well as feasible.

These, however, are short-term considerations. Everybody knows that in the 1980s, fast reactors will be the work horses of the nuclear power industry. Prudently enough, the Atomic Energy Authority has now commissioned its 250 megawatt fast reactor at Dounreay in Scotland, and the time is quickly approaching when the Central Electricity Generating Board will be able to place the first order for a fast reactor power station. The experience of the past few years has shown clearly enough, however, that the introduction of a new type of reactor entails a great deal of development cost and a great deal of technical uncertainty. On past experience, these considerations are likely to be a powerful brake on the speed at which new types of reactors can be installed. Anomalously, all the countries of Western Europe are being required to face the same problems independently but simultaneously. But is there not the most urgent need for some integrated attack on this common problem within the context of the European Communities? For it remains, as it has been for the past decade, a great waste of effort and of money that the European nuclear industry should be as fragmented as it has become. In present circumstances, there would be immense advantages in a vigorous coordination of European plans for developing fast reactors. This, too, is a matter on which the British government could take the initiative.

Defence Research

THERE is at least a chance that the most conspicuous gap in Lord Rothschild's recipe for public expenditure on research and development in Britain will now be filled. The defence estimates for the coming financial year, published last week (Cmnd 4891, HMSO, £0.47), laconically announce that the Ministry of Defence has embarked on a study of the defence research establishments and of the Atomic Energy Authority's Atomic Weapons Research Establishment at Aldermaston so as to rationalize their work and to make economies. By all criteria, this step is long overdue, and the defence estimates themselves make clear that there are potentially enormous benefits to be won from a reorganization of military research and development. In the year ahead, the Ministry of Defence

expects to spend £330 million on research and development, £122 million on military aircraft and £110 million on guided weapons and electronics. The numbers of people engaged on these activities are in excess of 30,000. Even though it is unlikely that reorganization will do much to divert money and resources from aircraft development, there are potentially great benefits to be won from a redeployment of the resources at present engaged in other kinds of military research, especially electronics.

The most serious defect in the present arrangements for defence research in Britain is the isolation of the defence research establishments from civil industry. Although the British government has for the past five years been seeking to encourage a closer relationship between the defence research establishments and the outside world, its attempts so far have not been conspicuously successful. The question that should now be asked at the Ministry of Defence is whether it will ever be possible to make the fullest use of the resources of these great establishments while they remain parts of the ministry as such. The difficulty, of course, is that military people are notoriously unwilling to strike a balance between what seems to them to be a sensible ordering of priorities and the wider considerations which might from time to time suggest that it would be better for the national interest if some civilian project were regarded more urgently. After all, the soldiers have been so chivvied in recent years by parliamentary committees which insist that new guided missiles or electronic systems or aircraft should be delivered on time, and have been made so self-conscious about their failures, that they have been reinforced in their belief that the defence of the realm, and the research and development which makes it possible, takes precedence over all other considerations. Yet the research projects on which £330 million will be spent in the coming year are not nearly as urgent as the ministry would like to think. Would it matter if the communications satellites which have been developed (and which are launched by American rockets) were replenished on precisely the schedule which has been laid down? Is it necessary that the ministry should be spending a substantial sum of money in the coming year on new communications systems for the forces when there is a crying need for more deliberate improvement of civilian facilities in precisely the same field? In short, there is a good case for asking whether the Ministry of Defence should not give projects like these a secondary place in what should be a national programme of research and development.

One immediate difficulty is that the Ministry of Defence and its research establishments are not at present organized for such a role. Even the largest of the establishments, such as the Royal Aircraft Establishment at Farnborough and the Radar Research Establishment at Malvern, function as if they are simple pensioners of headquarters in London. So long as the establishments are required to look to the ministry for detailed guidance on policy and even day-to-day management, it is unlikely that they will also be able to contribute creatively to the design of programmes of research and development in fields not directly within the responsibility of the ministry. It follows that the first step in making fuller use of the defence research establishments must be a devolution of responsibility from the Ministry of Defence to its research establishments. The transfer of the Atomic Weapons

Research Establishment to the Ministry of Defence should help in this direction, if only because Aldermaston has been less tightly knit within the Atomic Energy Authority than are the defence research establishments within the Ministry of Defence. In the long run, however, it could well turn out that the research establishments should be hived off altogether from the Ministry of Defence, and that they should in the process be converted collectively into a kind of research contractor, able and willing to accept research and development contracts not merely from the Ministry of Defence but from other government departments or from industry as well. Lord Rothschild's customer-contractor principle may be less palatable to the scientific community than to the government when applied to the research councils, but there could easily be more backing for its application to military research establishments.

What particular benefits would there be if the research establishments were more fully used outside the narrow field of defence research? Electronics and telecommunications would be most immediately affected. Even if research establishments such as the Radar Research Establishment were able more easily to act as research contractors for outside customers, the Post Office included, there is a good chance that the electronics industry would make good use of the service. But there is every reason why laboratories such as that at Malvern should be persuaded to follow the now successful pattern of development at the Atomic Energy Research Establishment at Harwell, where a laboratory once devoted to a single theme had been converted not merely to passive research contracting but also to industrial innovations in which the laboratory shares some of the financial risk and can expect to enjoy some of the rewards of success. This implies that hiving off of defence research from the direct control of the Ministry of Defence should be a preliminary to a much more radical liberalization of the ways in which these establishments function.

100 Years Ago



AT a late meeting of the State Dental Society of Pennsylvania one of the members, Dr. Barker, is reported in the *Dental Times* (July 1871) to have read an essay on Irregularity of Teeth, the circumstances favouring it, and suggestions on its prevention and treatment. The essayist held the opinion that a retrograde metamorphosis is going on in human teeth. To obviate this there must be improvement in the mode of living, the use of more substantial food, and from the time of the appearance of the deciduous teeth children should be under the care of an educated dentist; so that when the permanent teeth begin to erupt they may be properly guided, and a regular arch result. As a rule the first permanent molars should be extracted to make room for the succeeding teeth, for the jaws of the Anglo-Saxon race are shortening, and no longer have room for thirty-two teeth. How will this end?

From *Nature*, 5, 349, February 29, 1872

OLD WORLD

Medical Research Council on the Rack

THE Medical Research Council walked into a minefield last week when it chose to expose a fallacy in Lord Rothschild's now infamous table 4. In giving evidence before the Select Committee on Science and Technology the council pointed out that the sum ascribed to research into ageing — £9,000 — only represented a fraction of the actual amount that the MRC spent on problems of old age. Dr A. F. Lever, Director of the Blood Pressure Unit in Glasgow, said that responses to letters that he had sent to directors of MRC institutes the previous week showed, with several replies still to come, that more than £100,000 a year was being spent on this problem.

The Select Committee was amazed that to obtain this total Dr Lever had to write to the directors of units and that it could not be found out directly from the MRC. Both Mr Ronald Brown and Mr Kenneth Warren, men whose views lie at opposite ends of the political spectrum, said that this demonstrated that the Medical Research Council was not adequately meeting the present needs of government. Mr Airey Neave, the chairman, expressed some surprise that this had not been brought to the attention of the government chief scientist and that it had taken more than three months for the error to be exposed.

Dr J. A. B. Gray, Secretary of the council, defended the MRC's system for the classification of work, and stressed that the £9,000 mentioned by Lord Rothschild only took into consideration the work done at the National Institute for Medical Research, Mill Hill, on the lifetime of cells and that other problems that were particularly relevant to old age were classified under headings such as cardiovascular disease and lung disease with no direct reference to ageing. Dr Gray did say, however, that the council could quote a sum for research into ageing and old age research but that it would have to be extracted from several programmes.

The select committee was surprised that this argument had not been given in the MRC's submission to the Secretary of State for Education and Science on the green paper, but Dr Gray pointed out that the submission was not the last word on the topic and that further discussions with the department were planned.

With the enthusiasm of the select committee visibly waning in the fourth public session of evidence—only half of the members were present and one was considerably more interested

in his mail than the proceedings—it fell to Dr M. F. Perutz, Director of the MRC's Laboratory of Molecular Biology in Cambridge, to throw some light on the problem. He pointed out that it was impossible to solve the problems of medicine "head-on" and that the causes of diseases can only be discovered if scientists have a better knowledge of what goes on in the cell. The National Institutes of Health in Bethesda, Maryland, recognize this by having, apparently, several institutes that study different aspects of health, but according to Dr Perutz most of the work within the institutes is molecular biology.

Dr Perutz and Dr Lever thought that the customer-contractor principle would lower the morale of the scientist in Britain. In a particular laboratory in the United States, according to Dr Perutz, there is a sharp distinction

between people working on contracts and on grants; the contract people tend to be exclusively "9 to 5" scientists whereas the scientists on grants have the traditional university attitude of ignoring the clock. The fear that Dr Perutz and Dr Lever expressed was that wholesale implementations of Lord Rothschild's recommendations would see the same attitudes develop in Britain. In the circumstances it was disappointing that the session ended on a sour note with Mr Ronald Brown being distinctly rude to Dr Perutz by saying that it was disgraceful for him to suggest that scientists would become "clerkish" if a customer-contractor principle was instituted. Mr Brown was also unimpressed with the case put forward by the MRC and his final words were that there was no evidence to show that the council was meeting the needs of the country.

POWER GENERATION

What Role for Coal ?

COAL is a dying industry—so the pundits have been saying for years. And when the miner's strike is over, it is possible that the one industry to have suffered irreparably will be the coal industry.

Ten years ago the situation would have been much worse. In 1960-1 91 per cent of Britain's gas came from coal, as well as 84 per cent of the electricity. Today only 2 per cent of Britain's gas is made from coal while 73 per cent of electricity is still coal based.

The reason for the dramatic fall in the dependence of gas on coal is, of course, North Sea gas, and it is unlikely that the gas industry will require large amounts of coal again before the end of the century—the earliest that natural gas could run out.

But electricity's high dependence on coal is the result of government pressure on the industry to continue to use it to ease the rate at which the pits are run down. In their last annual reports both the CEBG and the Electricity Council complained that the tie to coal was forcing their prices up and their flexibility down.

The electricity industry has long fought the government on having to use so much coal, and it is likely that the latest crisis will result in renewed demands to be allowed to use natural gas for power generation and to convert more coal fired stations to dual oil and coal firing.

The writing has been on the wall for

some time. In the coal shortage which the CEBG became aware of in 1969, the government gave permission for five coal firing stations to be converted to dual oil and coal firing. Since then permission has followed for five more conversions in spite of the government's continued policy of supporting coal. In the past three years two stations have been converted to dual natural gas and coal firing with gas being used when it is plentiful, but in time of high demand the supply is cut off and the stations revert to coal firing.

One other clear sign of the CEBG's attitude to coal stations comes from its proposed building programme. Of the fifteen stations for which permission has been obtained or sought, only one is for a coal fired station, Drax II in Yorkshire. Consent has been granted for it, but ominously the CEBG has not gone ahead with construction.

In figures quoted by Mr E. S. Booth of the CEBG, 78 per cent of electricity will be generated by fossil fuels in 1980 with 22 per cent by nuclear power. By the year 2000 he conjectures that the figures will be 60 per cent nuclear and only 40 per cent fossil.

If the CEBG gets its way and is allowed to place greater dependence on oil—especially if the £2 a ton tax on oil is removed—and if the price of coal continues to rise, it is unlikely that coal will be playing that large a part in fuel generation by the end of the century.

COLLOID SCIENCE

Special Support Needed

THE Science Research Council considers that about £100,000 will have to be spent during the next two or three years if interest is to be revived in colloid science and if the subject is to be properly developed. The council says that, in the first instance, existing research groups should be strengthened and young workers encouraged to set up new and independent research teams. The justification for adding colloid science to the list of subjects considered worthy of special support by the SRC is contained in the report of a multidisciplinary panel set up by the chemistry committee of the council's science board and published last week (*Colloid Science*, Science Research Council: 1972).

Part of the panel's brief was to examine colloid science as practised in both academic institutions and industry, and a substantial part of the report is concerned with present manpower levels and the way in which they could be improved. The panel found that between 1955 and 1970 about 170 PhDs and 10 MScs by research were awarded in colloid science—most of them in chemistry departments, but a "substantial number" in chemical engineering, pharmacy and physics departments. The number of PhDs who qualified in chemistry departments during those years was 1.4 per cent of all PhDs in chemistry. And since 1964 about twelve students a year have graduated from the MSc course in surface chemistry and colloids at the University of Bristol.

Of the thirty or so postgraduate students with special knowledge of colloidal dispersions who have emerged from the universities in each of the past five years, more than half have entered industrial employment, according to the report. As for the manpower situation in companies themselves, it turns out that those principally concerned with chemicals have about 14 per cent of their research staff working on colloids, but only about 7 per cent of these were originally trained in the subject. On the other hand, companies involved with detergents or food technology tend to employ more specialist colloid scientists. The panel also says that it is "amazing that several organizations indicated that they had no interest in colloid science, although they are heavily dependent on materials exhibiting complex colloidal phenomena". This lack of awareness is, in the panel's view, partially a consequence of the absence of colloid science from many undergraduate courses.

One of the recommendations of the panel is that inter-university seminars should be held every two years to stimulate and maintain interest in col-

loid science, especially among holders of SRC postgraduate awards. The panel also suggests that there is a special role to be played by the SRC's Cooperative Awards in Pure Science scheme in forging channels of communication between those companies with an interest in colloids and the appropriate academic institutions. And the report calls on bodies such as the Society for Chemical Industry to recognize the need to disseminate information on developments in colloid science to all companies that should be aware of new developments and their possible applications.

Finally the report recommends that the SRC should set up an advisory panel to review progress and advise on future developments—in two or three years time, for example, this panel should be in a position to recommend what further financial support is necessary, and whether the closer cooperation hoped for between industry and academic institutions will require its own special funding.

CONSERVATION

Protection for Seals

WITH commendable foresight—no doubt prompted by the memory of the past history of the International Whaling Commission which arrived too late and too feebly to protect the blue whale from decimation (see *Nature*, 232, 80; 1971)—the first steps have been taken to protect Antarctic seals. At a conference in London recently, the twelve signatories to the 1959 Antarctic Treaty adopted the text of a convention forbidding the killing of Ross, elephant and fur seals, and limiting the slaughter of crabeater, Weddell and leopard seals in latitudes below 60 degrees south. The convention is designed to protect seals from commercial exploitation and for once governments have begun to move before industry.

Under the terms of the convention—which has yet to be signed and ratified—the species and numbers of all seals taken in the Antarctic must be reported to the Scientific Commission for Antarctic Research (SCAR). Limits to the numbers of seals that can be taken have been set and are well within the estimated maximum sustainable yield. Once these limits have been reached in any one year the signatories will meet again and consider what action can be taken. As all the early killings have to be reported to SCAR with details of age, sex and reproductive condition, it is hoped that by then scientists will have a much clearer idea of the numbers of seals in the area.

Current estimates vary from 5 to 50 million. Estimating numbers is difficult as the Antarctic covers one fifth of the

world's surface, and the seals, with the exception of the Weddells, tend to live in the sea rather than on land or fast-ice. The most common species is the crabeater with an estimated population between 2 and 10 million although there may be many more. The limits that have been set to catches are 175,000 crabeater seals, 12,000 leopard seals and 5,000 Weddell seals.

These moves come before seals are in danger. There has only been one commercial expedition to the Antarctic in recent years—by the Norwegians—and there is no industry established yet. The seals, however, represent a valuable resource as their blubber oil is very similar to whale oil and can be used for solid oils and cooking fats, and scientists are convinced that it is only a matter of time before industry moves into the Antarctic. They hope that potential exploiters will see the convention as a declaration of intent, and thus it will prove possible to control the industry before large amounts of capital are involved. It is this as much as anything which made the International Whaling Commission ineffective, as industry was heavily involved financially before attempts were made to control it.

The British representatives at the conference are well pleased with the results. Dr Brian Roberts of the Polar Regions Section of the Foreign and Commonwealth Office said last week that the convention was "a very big step forward" and Mr Nigel Bonner of the Seals Research Unit, Lowestoft, also said last week that the convention forms "a very adequate safeguard".

The reaction of bodies not actually involved in the convention is not so enthusiastic. Both the World Wildlife Fund and the Fauna Preservation Society welcome the convention as providing some sort of protection where before there was none. But both wish the agreement had more teeth. There is no provision for observers in the convention, although it is stated in the text that they may be introduced at the next meeting, when the catch limits have been reached.

It is, however, no secret that the convention is something of a compromise. The Americans came to the conference hoping for some sort of inspection system and even added a statement to the text saying "that the convention should contain stronger provisions for the observation of operations and enforcement of regulations". Agreement on this proved impossible largely because the USSR, Chile and Argentina would not agree to inspection of their vessels; the South American countries, because they claim territorial waters 300 miles off their coasts, would not agree to inspection within them. As it is, however, the reporting system to which the contracting parties have

agreed is fairly comprehensive and there are clear provisions for revising and strengthening the agreement once an industry is established.

Further, all the nations likely to be involved in sealing have adopted the convention, with the exception of Canada which was not a signatory to the 1959 Antarctic Treaty, but is expected to sign the convention. As one British Foreign Office official said last week "you can either have a convention that's perfect and signed by the wrong people, or one that's imperfect but signed by the right people".

ASTRONOMY

Changes at Cambridge

THE appointment, announced last week, of Professor Donald Lynden-Bell to succeed Professor R. O. Redman in the chair of astrophysics at the University of Cambridge has been welcomed among the astronomical community in Britain. This is not only because of the skills which Professor Lynden-Bell brings to Cambridge, but because the appointment also provides the first indication of the way in which the new Institute of Astronomy might develop.

In July 1971, the merger of the Institute of Theoretical Astronomy and the University Observatories into the Institute of Astronomy was announced to take effect from August 1972. In part, the decision was made then because of the impending retirement of Professor Redman, Director of the Observatories, and the recent retirements of Dr H. von Klüber, Assistant Director of the Solar Physics Observatory, and of Dr E. H. Linfoot, Assistant Director of the Observatories.

Under the new arrangements the Director of the Institute of Astronomy will be appointed from among the professors of the institute for a period not exceeding five years. In all probability, the first director will be Sir Fred Hoyle, Plumian Professor of Astronomy and Experimental Philosophy, and currently Director of the Institute of Theoretical Astronomy. But, as Professor Astrophysics, Lynden-Bell will be a member of the advisory committee which will run the new institute, and in due course he may be expected to take his turn as director.

How might this new appointment be interpreted with regard to the future of astronomy in Cambridge? It is perhaps significant that Professor Lynden-Bell has interests ranging from problems connected with the overall structure of the universe to the structure of galaxies and the construction of telescopes. Although he modestly claimed last week that his experience of practical astronomy was "completely negligible", he has, in fact, worked closely

with observers at the Royal Greenwich Observatory, where he has been a Senior Principal Scientific Officer since 1965. This collaboration exemplifies how many people hope the new institute will develop. Professor Lynden-Bell also sees the development of strong links between the astronomers at the new institute and the radio astronomers at the Cavendish Laboratory, which will soon be moving to a new site near the institute.

It is interesting that Professor A. H. Cook, now at the University of Edinburgh has been appointed Jacksonian Professor of Natural Philosophy at the Cavendish with effect from October 1, 1972. Professor Cook's interests in spectroscopy and instrumentation encourage the speculation that there might well be collaboration on the problems of optical astronomy, as well as on the problems of radio astronomy. In spite of some doubts about the future of the highly successful programme of visiting fellowships which has helped to place the Institute of Theoretical Astronomy in the forefront of world astronomy, it seems that the future of astronomy within the University of Cambridge is assured.

Sir Brian to Stay

SIR BRIAN FLOWERS will continue as chairman of the Science Research Council for a further three years after his term of office expires next September. The announcement, made last week, has stilled speculation that Sir Brian would return to academic life at the end of this year but even though he has resigned his position as Langworthy Professor of Physics at the University of Manchester he said last week that this does not mean that he is completely shutting the door on the academic world.

Sir Brian said that the major reason for his acceptance of the invitation to stay on as chairman of the SRC is "to steer the SRC and the research council system generally through this difficult and confused period". He will strive to ensure that the white paper that the government is to publish on the future of government research development will be acceptable to the scientific community.

There is no doubt that a new man at the helm of the SRC at the end of this year would have created difficulties for the council in implementing any changes necessitated by a change in government policy. The scientific community will welcome Sir Brian's extended stay in command.

POLLUTION

A Clean Sea

TWELVE European countries, including Britain, signed a convention in Oslo last week aimed at preventing ships and aircraft from dumping waste indiscriminately in the North Sea and parts of the North-East Atlantic and Arctic oceans.

Under the convention—which has yet to be ratified—the dumping of substances likely to find their way into the food chains is completely prohibited—these include organohalogen and organosilicon compounds, carcinogenic substances, mercury, cadmium and persistent synthetic materials. The dumping of certain less harmful substances will be allowed under certain well defined conditions but only if a permit is obtained from the relevant national authority. If material is dumped, it must be unloaded into a depth of not less than 2,000 metres at least 150 nautical miles from land.

Mr James Prior, Minister of Agriculture, Fisheries and Food, said that as far as Britain was concerned the convention would simply make legal the conditions and prohibitions under which British industry had already been operating by voluntary agreement. It does, however, ensure that all the countries involved will live up to the same standards. Asked what penalties there would be for ships breaking the agreement, Mr Prior said that these would not be fixed until the ratification of the convention by Parliament (which should take place next session) but they will be "very severe". A commission is to be set up to oversee the working of the convention.

The area covered stretches westwards to Greenland and southwards to near Gibraltar but the agreement excludes the Baltic and Mediterranean seas. Dr Herbert Cole, Director of the Fisheries Laboratory at Lowestoft, said that he hoped the present convention would be followed by agreement in these areas.

Mr Prior pointed out that he and the other signatories were well aware that most pollution in the sea comes from rivers and pipelines. Urgent consideration is being given to controlling these sources, however, and he felt that the dumping convention was "a convenient starting point to deal with the broader problems".

The convention could be the first of a series of international agreements over the next few years to protect the sea and fisheries. A United Nations intergovernmental committee is discussing world anti-dumping measures which can be expected to follow the same principles as the present convention, and future agreements on the carriage of potentially dangerous cargoes may also result.

NEW WORLD

End of the Road for NERVA

by our Washington Correspondent

AFTER spending about \$1,400 million over sixteen years on the development of a large nuclear engine for space vehicles, the US Administration has finally decided to cut its losses and abandon the project. Much to the chagrin of some members of Congress and at least one Atomic Energy Commissioner, the Office of Management and Budget has stripped all funding for NERVA (Nuclear Engine for Rocket Vehicle Application) from the budgets of the Atomic Energy Commission and the National Aeronautics and Space Administration, and the project is probably doomed even if Congress follows past precedents and puts the money back into the budgets.

Officials of the Atomic Energy Commission last week appeared before the Joint Committee on Atomic Energy to discuss the Administration's decision to axe NERVA: most kept a stiff upper lip and insisted that the decision is justified, since there is no longer a requirement for such a large nuclear rocket. But Commissioner James T. Ramey, himself a past staff member of the Joint Committee, made no secret of his disappointment at the Administration's handling of NERVA: "For something like an additional \$400 million," he said, "we can proceed with confidence through a flight test and give the United States an unquestioned place of leadership in space." At the very least, Ramey suggested that the Joint Committee should vote \$20 million to keep the project ticking over.

Whether the Joint Committee will follow Ramey's advice is a moot point, and it is probably academic in any case. Last year there was no question that the committee would authorize the expenditure of more money for NERVA than the Administration requested, but precisely because this support for the project was thwarted by the Office of Management and Budget, the ground rules have changed and the Administration may well kill the project without too much of a fight.

What happened last year was that in spite of strong support for NERVA from both NASA and the AEC, the Office of Management and Budget sent to Congress a request only for sufficient funds to keep the project ticking over. The Joint Committee on Atomic Energy, the Senate Committee on Aeronautical and Space Sciences and the House Committee on Science and Astronautics all authorized sufficient expenditure to allow NERVA develop-

ment to proceed at a pace, but OMB refused to spend all the money, and the project was wound down. This year, with strong pressure on NASA to keep its budget approximately constant over the next few years, NERVA got squeezed out completely and Congressional committees are aware that decisions have already been taken to reduce staff levels in the two chief NERVA contractors, so that no matter what funding is authorized for the project in 1973 it will probably not be spent by the Administration.

Designed to move large payloads from low Earth orbit into geosynchronous orbit, or further afield to the Moon and planets, NERVA is being killed chiefly because there is not sufficient requirement for such a large vehicle in the early 1980s, when it would have been available. That, at least, was the argument put forward last week by David S. Gabriel, director of the Space Nuclear Systems Division of the AEC, in testimony before the Joint Committee on Atomic Energy. Gabriel assured the committee that the technology would not be lost, however, for if the need for NERVA arises in the future, it would be possible to build on the existing technology base and have a nuclear engine ready for flight testing in a comparatively short time.

But the chief benefit from the \$1,400 million spent on NERVA is likely to occur in the development of a much smaller nuclear engine for a spacecraft that will be capable of reaching the outermost planets in the 1980s. When James T. Fletcher, administrator of NASA, announced the cancellation of the Grand Tour of the outer planets, he pointed out that NASA and the AEC had undertaken to develop a nuclear powered outer planets spacecraft so that the option of visiting the planets beyond Saturn is not completely foreclosed this century. Similarly, Gabriel said last week that NERVA technology will be invaluable in building the mini-NERVA, as it has been dubbed. (The scaled down version would have a thrust of about 15,000 lb compared with the 75,000 lb thrust of NERVA.)

In spite of these assurances, however, it became clear last week that the Administration has not yet made a definite decision to develop a small nuclear engine. Gabriel said later in his testimony that such an engine is only one candidate for outer planetary missions, and that a study will soon be carried out to determine what sort of propulsion

system will be developed for space missions in the 1980s. Systems under consideration include advanced chemical rockets, nuclear-electric and solar-electric propulsion and nuclear propulsion.

Of those four options, nuclear-electric is the least advanced, solar-electric would not be practical for outer planetary studies on the fringes of the solar system because the Sun's power would be too weak, and so the final decision may well boil down to a choice between advanced chemical and nuclear propulsion. As far as costs are concerned, Gabriel tentatively suggested that nuclear-electric, nuclear and advanced chemical propulsion would each cost about \$400 million to develop, while solar-electric technology may be available for an outlay of about \$100 million. To carry NERVA development through to completion, on the other hand, would cost about \$500-600 million. Gabriel told the committee that funding levels for the engine programme will undoubtedly increase from the level proposed in the 1973 budget, when various designs have been studied and a commitment is made to one type of engine.

One rather ironic aspect of the cancellation of NERVA is that development of the engine has been tied to development of the shuttle—because of the very slight danger of radioactive release from the engine, NERVA would only have been used outside the Earth's atmosphere and the thinking was, therefore, that it would have been launched from the shuttle. It would also have been a useful means for carrying heavy satellites from the low orbit of the shuttle to synchronous orbit or to the Moon for later lunar exploration. Now that the shuttle has been given the go-ahead (Congress willing), however, there is not enough money available for NERVA. As Gabriel said last week, NERVA needs the shuttle, but the shuttle does not need NERVA.

MARIHUANA

Pot and Health

by our Washington Correspondent

THE possibility that smoking marihuana can be damaging to health has for long been the basis of exaggerated claims and counter claims as the debate over the drug's legal status has intensified in the United States. And, since any aspect of the drug always makes for good copy in the press, the American

public is understandably confused by what seem to be widely conflicting reports of the safety of marihuana use. A report prepared by the National Institute of Mental Health and presented to Congress last week, however, provides a welcome relief from the rhetoric.

An extensive and detailed survey of the scientific literature on the health effects of marihuana, the report makes few definitive statements, and steers well clear of any discussion of the legal status of the drug. Nevertheless, the tenor of the report was best summed up by Dr Bertram S. Brown, director of the National Institute of Mental Health, who said at a press conference last week that the evidence so far indicates that "in a healthy subject taking moderate doses, there seems to be no harmful effects". But Dr Brown was also quick to point out that conclusions about the safety of marihuana are necessarily tentative and much more research into its possible chronic effects is required before sound inferences can be drawn.

The report addresses itself chiefly to a consideration of research results that have been reported during the past year, and it is clear that one of the most important advances has been the development of synthetic forms of the chief active ingredient, delta-9-tetrahydrocannabinol. Research into marihuana use has long been dogged by the difficulty of determining dose rates and the related difficulty of providing comparability in experiments.

Nevertheless, the report has many comforting things to say on the basis of studies so far. As far as acute toxicity is concerned, for example, experience with animals and in man has shown that extremely large doses are required before any dangerously toxic effects are noted. In animal studies, the minimum lethal dose of delta-9-thc that causes death is about 1 g/kg administered orally, and it is not possible to find an LD₅₀ for these animals. Similarly, in man, there have been extremely few reports of death from an overdose of marihuana and those that have been reported are almost invariably doubtful in some aspects.

Attention has therefore been focused chiefly on the possible chronic effects of long-term marihuana use. Here again, the report seems to suggest that chronic effects, at least with moderate use, are slight. The most common physiological change from smoking marihuana is an increase in pulse rate and a reddening of the eyes, but these effects are relatively short-lived, lasting for only an hour or so after using the drug. The effect on respiratory complaints is often complicated by the fact that marihuana is often mixed with tobacco, but one study among Ameri-

can troops in Germany has found evidence of bronchitis, asthma and throat inflammation which disappeared when use of the drug discontinued. There is little evidence of impaired liver function or circulatory disability that can be pinned down to marihuana use alone, and the report notes that studies of heavy users of hashish in Greece and Jamaica, some of whom had used the drug daily for up to 20 years, provided no real indication of chronic effect. This finding was cited last week by Dr Robert Peterson, who was chiefly responsible for compiling the report, as being particularly surprising to him.

Perhaps the most serious indication of damage from long-term use of marihuana is the recent report of brain atrophy in ten young cannabis smokers. But the report suggests that this finding is inconclusive since most of the subjects were multiple drug users. Some investigators have also doubted that the

radiographic techniques used in the study are suitable for detecting cerebral atrophy. Nevertheless, the report suggests that the importance of the finding clearly merits considerable further study.

As for the possible teratogenicity of marihuana, the report cites two animal studies that have failed to come up with evidence of birth defects, and there is no evidence so far that marihuana use is likely to cause chromosome breakage. Moreover, "the number of clinical reports of birth defects in children of mothers who use cannabis has been very small, especially considering the large number who are believed to have been exposed to the drug". But only a few preliminary studies have been reported and the report cautions that since the teratogenicity of the drug cannot be completely evaluated, its use would be unwise among women during their reproductive years.

AGRICULTURAL RESEARCH

More Aid to Green Revolution

by our Washington Correspondent

THE green revolution has received its first direct support from the World Bank in the shape of grants amounting to \$1.26 million for international agricultural research institutions. The grants, which were awarded earlier this month, are part of some \$15 million that is being made available in 1972 for international research projects by members of the newly-formed Consultative Group on International Agricultural Research.

The World Bank grants mark the first tangible signs of the efforts of the Consultative Group to channel more funds into internationally supported research centres aimed at increasing the quantity and quality of food production in developing countries. Chief beneficiary of the World Bank's entry into agricultural research is the International Wheat and Maize Improvement Centre in Mexico, which is set to receive \$1 million, while the International Potato Centre in Peru has been given \$160,000 to help with projects designed to breed a variety of potato with an enhanced resistance to disease and which can adapt to tropical climates.

Behind the formation of the Consultative Group on International Agricultural Research, and the subsequent awarding of the World Bank's grants, lies the suggestion that although the so-called green revolution has received a good deal of public attention, not to mention a Nobel prize, it has been in danger of running short of funds. In any case, in 1970 it seemed that the growth and size of the five internation-

ally supported agricultural research centres were such that their traditional sources of funding would be inadequate to meet their financial needs. Until then, the research centres were supported chiefly from North America, with the Ford, Rockefeller and Kellogg Foundations, together with the US Agency for International Development, providing the bulk of the finances.

A meeting convened by the United Nations in 1970 to discuss priorities and funding for international agricultural research led indirectly to the setting up of the Consultative Group, whose members include the Ford, Rockefeller and Kellogg Foundations, the FAO, the UN development programme, the World Bank, the twelve donor governments (Belgium, France, Germany, Japan, The Netherlands, Norway, Sweden, Switzerland, the United Kingdom and the United States) and representatives from five developing regions. At a meeting in December last year, the group agreed on a programme of support for the five existing research centres.

The World Bank grant includes a donation of \$100,000 to a fund to set up an International Crops Research Institute for the semi-arid tropics which will probably be based in India, and when the group next meets in the autumn it will decide whether to set up a centre in Africa for the improvement of cattle production. The group is advised by a committee of twelve scientists under the chairmanship of Sir John Crawford, vice-chancellor of the Australian National University.

NEWS AND VIEWS

Climatic Records from Ice Sheets

OXYGEN isotope profiles through the entire depth of the ice sheets of Greenland and Antarctica have already been shown to provide an excellent record of climatic changes which are similar in timing and character to the main changes recorded elsewhere in the northern hemisphere by other methods. Potentially, the oxygen isotope δ values provide a more sensitive and more continuous profile of changes during the past 10^5 years than is available by any other method. This has been shown by detailed profiles for the Greenland ice sheet (W. Dansgaard, *Science*, **166**, 377; 1969) and for the Antarctic (Epstein *et al.*, *Science*, **168**, 1570; 1970). Epstein *et al.* also showed that hydrogen-deuterium ratios changed in step with the oxygen δ values. Dansgaard's group (*Nature*, **227**, 482; 1970) have used analysis of their data for the past 800 years to determine periodicities in climatic oscillations, and hence to predict climatic trends.

Although the method is extremely effective in recording small fluctuations of climate in terms of changing δ values, there remains a weakness in dating the various events recorded in the profiles. Development of carbon-14 dating of ice at various depths by *in situ* methods of extraction of carbon dioxide from the ice promises in due course an independent method of dating ice cores. At present, however, dates are estimated from various modifications of the steady state theory of the deformation of ice sheets. The new report by Johnsen, Dansgaard, Clausen and Langway on page 429 of this issue of *Nature* shows that variations of δ value along the core from Camp Century, Greenland, could, in principle, be used to determine absolute dates of various layers by direct counting of the summer and winter layers in much the same way as is done for varve clays. Their results show that although the seasonal amplitude of δ values is around 10 per mille in freshly deposited snow in north-west Greenland, as the snow is consolidated into firn a smoothing and filtering of δ values take place as a result of sublimation processes in the porous firn. The seasonal amplitude is reduced to around 2 per mille and shorter period variations are eliminated in ice of 280 years age at 115 m depth. By 100 m depth the ice is no longer porous so that there is little change in amplitude below that level until diffusion processes become effective. These take place in the Camp Century core at about 1,000 m depth (total depth 1,390 m) in ice around 6,000 to 8,000 years old, when the annual layers have been squeezed from 35 cm thickness to about 5 cm.

In practice, use of a mass spectrometer to determine a large quantity of δ values is a relatively expensive and lengthy task. Johnsen *et al.* estimate that a sampling interval of about one-eighth of an annual layer is necessary for satisfactory identification of layering. Some 70,000 measurements would therefore be necessary to trace all layers in the past 8,500 years. This task is an order of magnitude greater than the already impressive accomplishments of Dansgaard's group, but continuous profiling of the material now available is also prevented by lack of continuity in the core, because of various breaks and shattering in the drilling process.

Johnsen *et al.* also report results on the core from Byrd station, Antarctica. They first attempted to see if it is possible to determine the annual layering in the core from seasonal fluctuations of δ values, but, as other workers have found elsewhere in Antarctica, regular seasonal variations of δ value are not sufficiently distinct in areas of relatively low precipitation for such use. Surprisingly, an apparently regular seasonal layering over a period of four years appears at 1,387 m depth in ice layers 5 cm thick corresponding to an age around 15,500 years BP. It seems likely therefore that locations may be found where annual layering can be usefully determined to somewhat greater ages than the 8,300 years found as the limit at Camp Century.

The second part of Johnsen *et al.*'s article discusses results of the authors' 3,000 determinations of mean δ values for the Byrd station core, taken over core lengths corresponding to periods ranging from 12.5 to 100 years. These present the important basic data for the core in more detail than the 80-odd determinations given in Epstein *et al.* (*Science*, **168**, 1570; 1970). Although there is general agreement between the results of the two groups, the greater detail in the later work sets Johnsen *et al.* on the trail of relating individual climatic events in the Byrd core to similar events in the Greenland core and elsewhere. It is clear from the three different models of flow of the ice sheet near Byrd station presented as possibilities by Johnsen *et al.*, plus the separate interpretation of Epstein *et al.*, that uncertainty exists as to how far up the flow line above Byrd station ice at various depths in the core originated. It also seems likely that during the period of nearly 10^5 years covered by the ice core, directions of ice flow near Byrd station may have varied significantly.

In spite of these uncertainties, the basic data present detailed quantitative evidence which is of great importance to the interpretation of past climatic events. The importance of the data will grow considerably when it can be dated more accurately and related to the past flow conditions. As more such records of δ values are obtained from different locations, it should be possible to correlate individual climatic events between the different cores, and thus improve confidence in the dating process.—From a Correspondent.

The Limits of Palaeogravity

A. D. STEWART's recent attempt (*Nature*, **235**, 322; 1972) to define the limits of long-term variation in the gravity field is important not only for what it has achieved against heavy odds but no less for the potential significance of the phenomenon it was designed to elucidate. It is now more than 30 years since Dirac (*Nature*, **139**, 323; 1937) first suggested on cosmological grounds that the so-called gravitational constant (G) might be decreasing slowly with time. He proposed that G varies inversely with time, a relationship which Gilbert (*Mon.*

Not. Roy. Astr. Soc., **116**, 684 ; 1957) much later showed to be consistent with the general theory of relativity and which Dicke (*Phys. Today*, **20**, 1 ; 1967) interpreted numerically as a reduction in G of about 1 part in 10^9 or 10^{10} per year. But no experimental confirmation of such a decrease has yet been obtained ; and in one sense the chances of so doing have now become even more remote. For three years ago, Faytel'son (*Dokl. Acad. Nauk SSSR*, **188**, 579 ; 1969 ; and **189**, 1240 ; 1969) showed that gravitational acceleration (g) has been varying in the Soviet Union with mean rates over a decade of about 1 part in 10^7 per year.

What is clearly required is some gravity-controlled process which will enable mean palaeogravity to be determined at various points throughout geological time. Unfortunately, a suitable process has proved elusive. There is, to be sure, no shortage of gravity-controlled phenomena—many geological processes, for example, fall into this category. But the problems are, first, that gravity seldom leaves a permanent record in the rocks concerned and, second, that the effects of gravity are usually small compared with those of other, often unpredictable, variables involved. It is here that the contrast with, say, palaeomagnetism is particularly marked. Palaeomagnetists have been lucky in that the acquisition of rock magnetization is subject to basically only one parameter—the direction of the ancient geomagnetic field—and in that, once acquired, such magnetization is usually remarkably immune to subsequent environmental influences, not least to later magnetic field variations. The determination of palaeogravity from geological processes, on the other hand, is likely to require a fairly detailed knowledge of the contemporary environment together with the changes which have taken place since.

Among potentially suitable phenomena (both geological and biological) suggested some time ago by Stewart (in *Palaeogeophysics*, Academic Press, London and New York ; 1970) are the gravitational compaction of clays, the compaction of clays beneath glacial ice, palaeobarometry, the size of flying animals, the depth of animals' footprints, the dimensions of the frames of land animals and the growth of diapiers. The last of these offers a particularly clear case study of the traps to be encountered in palaeogravity determination.

Salt diapiers, or salt domes, are particularly numerous in the sediments of the Gulf of Mexico, though they also occur elsewhere, and have recently been discovered in some profusion in the floor of the Mediterranean. In such places where salt deposits have been deeply buried, salt is sometimes squeezed upwards where the sediment cover is comparatively weak to form plugs, or domes, which may rise several kilometres and even, on occasion, pierce the sedimentary surface. Assuming that the only forces acting on the salt are gravitational, the upthrust in a salt dome may be written as a simple expression involving g , the height of the dome and the densities of the salt and sedimentary overburden. This upthrust is resisted by the weight and strength of the sediment cover immediately above the dome ; and the thickness of this cover will, according to the simple gravity model, decrease as the diapir rises under gravitational forces. For a population of salt domes in a given area, the proportion of domes reaching a given level should thus be a function of gravity. Measurement of this proportion for salt domes of different ages should then show the way to

a relative measure of the variation of g through time.

The snags in applying this simple model are only too clear, because gravity is unlikely to be the only operative variable in practice. For one thing, if purely local effects are to be discounted, the members of the salt dome population envisaged above must all lie in an area of uniform sedimentation. Alternatively, local effects should be eliminated statistically by measuring many different populations of the same age. Moreover, as Barton (*Bull. Amer. Assoc. Petrol. Geol.*, **17**, 1025 ; 1933) pointed out long ago, the growth of salt domes may depend on the local rate of sedimentation, in which case the distance between the top of a dome and the sedimentary surface could well remain roughly constant even as the dome grows. Finally, an increase in g subsequent to dome formation could result in the reactivation of extinct domes—a particularly relevant effect if the variations reported by Faytel'son prove to be world-wide. All of which probably explains why attempts to analyse natural data combined with results from laboratory model studies have led to obviously erroneous palaeogravity values—for example, that palaeogravity over the past few hundred million years has been 10–100 times lower than at present.

The technique developed by Stewart, and reported in *Nature* two weeks ago, has been rather more successful than this, however, not in determining accurate values of palaeogravity but in defining a limit in the decrease of g with time which, though broad, is not inconsistent with theoretical prediction. The method itself involves the measurement of the degree of overconsolidation in sediments which, though once buried beneath other sediments, have been exposed by erosion. The basic idea here is that for a given thickness of sedimentary overburden, the compaction will be greater the higher the value of g . Thus if g were higher in the past, sediments would be overconsolidated with respect to present-day sediments.

Stewart's results clearly show that the London Clay now exposed has been consolidated by higher pressures than would have been produced by what is now the greatest thickness of sediment overburden to be found anywhere in the London basin. It is quite possible, of course, that this extra pressure was derived from sediment younger than any now observed, additional overburden which has since been eroded away. But if the additional pressure was generated solely by a higher value of g in the past (actually about 26 million years ago), the figures are such that gravity at that time could not have been more than twice its present value. If the actual thickness of the additional overburden, if any, were known, the limit on the ancient value of g could be tightened considerably. In the meantime, however, Stewart is able to rule out any decrease in g greater than 4 parts in 10^8 per year over the past 26 million years.

A decrease of g or G with time, even if several orders of magnitude lower than the maximum limit set by Stewart, would clearly be of central importance in cosmology and planetary theory. For the Earth scientist, on the other hand, the significance of a possible long-term decrease in G lies in the unresolved, and problematic, question of the Earth's expansion over geological time—the point here being that a decrease in G would inevitably lead to a significant expansion unless an unrelated process produced an equal and opposite effect.—P. J. S.

JUPITER

Probing by Pioneer

by our Cosmology Correspondent

THE most distant journey of exploration so far attempted is due to begin soon with the launch on February 27 of the Jupiter probe Pioneer F from Cape Kennedy. If all goes well, this two year mission will send back data from interplanetary space and the asteroid belt before flying by Jupiter at a distance of 87,000 miles. Pioneer will not enter orbit around Jupiter, however, but will continue through the outermost regions of the solar system, eventually escaping altogether from the Sun's influence. As well as the importance of the Jupiter mission itself, this marks another great step forward in the history of space exploration, with Pioneer F eventually becoming the first man made object to travel in interstellar space.

Experiments carried by Pioneer F will study magnetic fields and cosmic rays in interplanetary space, as well as observing the atmosphere and magnetic field of Jupiter. The continued success of spacecraft such as Mariner 6 and Mariner 7 long after their planned lifetimes had expired shows that the difficulties of constructing instruments which can function in space for years have been largely overcome. Where the Pioneer project is breaking completely new ground is in the distance over which communication must be maintained, and in the use solely of nuclear power to generate the electricity to run the experiments and maintain com-

munication with the tracking station.

Because of the communication problem, Pioneer F appears almost to be an interplanetary radio antenna with a few experiments stuck on the back (see figure); once in space the four radio-isotope generators used to provide electricity will be deployed at the ends of long booms, removing them from the sensitive experiments and giving the craft a rather more balanced appearance. This power supply, which is similar to those used for Apollo experiments left on the Moon, has a design lifetime of five years. Past performance suggests, however, that they will last for much longer, and although it is extremely likely that contact with the Pioneer will be lost long before it reaches the edge of the solar system, it seems reasonable to expect a continuing flow of data for some time after the close approach to Jupiter.

Depending on the exact date of the launch (the launch window is from February 27 to March 13), the craft will arrive at Jupiter, if all goes well, sometime between October 1973 and June 1974. A similar mission, Pioneer G, is scheduled for launch in April 1973.

NUCLEIC ACIDS

Silk Messenger

from our Cell Biology Correspondent

IF there is one lesson to be learnt from the recent history of biology it is surely that if the biologist is to answer questions of the most general biological significance he must have a talent for selecting the most appropriate experimental system or organism; he must not only know what questions are important but also where best in the plant and animal kingdoms to start to seek answers. The work reported by Suzuki and Brown in the current issue of the *Journal of Molecular Biology* (63, 409; 1972) shows clearly that these authors have that talent in full measure.

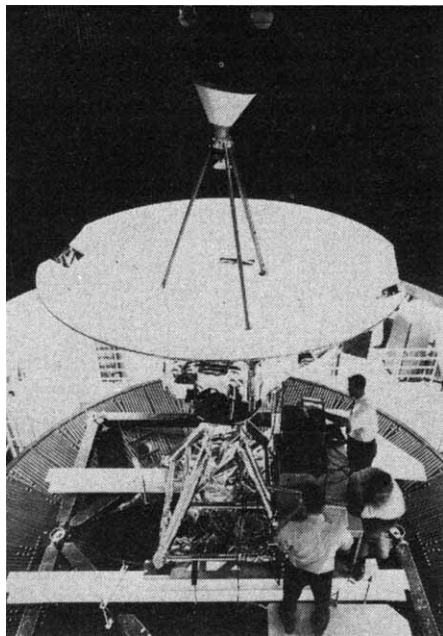
Suzuki and Brown, like many another group these days, wanted to isolate and purify a messenger RNA species from a eukaryotic cell with the ultimate aim of investigating its synthesis and metabolism. But instead of following the already overcrowded paths leading to reticulocytes and myelomas, Suzuki and Brown turned their attention to the silkworm *Bombyx mori*. The larvae of this insect secrete fibroin, silk protein, of which no less than 45 per cent of the amino-acid residues are glycine and in silk the glycine residues alternate predominantly with alanine and serine residues. Furthermore, the fibroin is made in the posterior silk glands of the larvae which can be dissected from the rest of the carcass.

A simple calculation, using known codon assignments, leads to the predic-

tion that fibroin messenger should have a G+C content of at least 57 per cent and a G content of about 40 per cent. It should therefore be possible to extract from the silk glands of larvae an RNA with this most unusual base composition. After labelling for 24 hours with ^{32}P -ortho-phosphate fifth day fifth instar larvae, Suzuki and Brown sure enough were able to isolate an RNA sedimenting at between 45S and 65S which proved to contain 59 per cent G+C residues, 40 per cent G residues and 19 per cent C residues. This RNA, which accumulates slowly and is more stable than either heterogeneous nuclear RNA or ribosomal precursor RNA, comprises, at the end of larval life, 0.8 to 1.4 per cent of the total RNA in the posterior silk gland, the only organ from which it can be isolated.

After partially purifying their putative fibroin messenger by polyacrylamide-agarose gel electrophoresis, Suzuki and Brown compared the pattern of oligonucleotides liberated from it during digestion by RNAase T1 or pancreatic RNAase with the pattern which can be predicted by writing out a base sequence for fibroin messenger knowing its amino-acid sequence and using accepted codon assignments. The products of digestion so closely match those predicted that there can be no doubting that the isolated RNA is at least 80 per cent pure fibroin messenger in which glycine is coded by GGU and GGA, alanine by GCU and serine by UCA. As Suzuki and Brown comment, the posterior silk gland of *Bombyx mori* larvae offers many advantages to anybody intent upon unravelling the synthesis, maturation, transport and translation of a specific messenger RNA. No doubt many a biochemist will be seeking a crash course in insect anatomy and Japanese exporters of silkworms can look forward to a boom in demand.

In the same issue of the *Journal of Molecular Biology* (*ibid.*, 575), Schochetman and Perry report a series of pulse labelling experiments which indicate that in L cells in culture RNA molecules which are tentatively identified as histone messengers are transported from nucleus to cytoplasm at an unusually rapid rate. Within 2.5 minutes of labelling with a pulse of ^3H -uridine, RNA with a molecular weight of about 150,000 can be extracted from cytoplasmic polysomes; RNAs with a higher molecular weight (10^5 to 2×10^6) appear in the polysomes only after a lag of about 15 minutes. Schochetman and Perry suggest therefore that very rapid transport to the cytoplasm can be added to the two other characteristics of putative histone mRNAs, namely their short half life and their synthesis during the S phase of the cell cycle.



Pioneer F being prepared for tests prior to launch. Information about the outer regions of the solar system may well be obtained from the craft for seven years, until it reaches a distance of some 2.4×10^9 km from the Sun.

RIBOSOMES

Pedigree and Parturition

from our Molecular Biology Correspondent

THE life cycle of the ribosome, from the ovum to the grave, as it were, is now almost fully documented, and makes one of the more absorbing stories of molecular biology. It begins with the ribosomal genes in the cellular DNA, which are present several times over in the bacterial genome, and hundreds of times in the eukaryotic chromosome. Denaturation maps of eukaryotic ribosomal DNA make this string of identical genes manifest: in this technique the DNA is held at a temperature within its melting range, the melted regions are propped open with formaldehyde and the population of molecules on a grid is examined in the electron microscope. The melted regions, which will have a lower content of (G+C) than those which remain intact, may then be indexed along the chain, when a repeating unit, consisting of (A+T)-rich regions, interspersed with those of high (G+C) in a characteristic pattern, may be seen. Such denaturation maps have been prepared, for instance, for the ribosomal DNA of *Xenopus laevis*. They show a four-peaked profile followed by a featureless tract of rather high (G+C) content. This last corresponds to the "spacer" region, which is eliminated when the 40S precursor RNA is broken down into the 18 and 28S ribosomal subunit RNA species, which comprise the greater part of the ribosomal gene.

Brown, Wensink and Jordan (*J. Mol. Biol.*, **63**, 57; 1972) have now followed up this earlier work by a comparison of the denaturation maps of *X. laevis*, and the closely related *X. mulleri*. The mature ribosomal RNAs of these species are, not surprisingly, identical within the limits of technique in base compositions, as well as physical properties, such as sedimentation and electrophoresis rates and absorbance melting curves. The buoyant densities of the ribosomal DNAs of the two beasts, however, are not identical, and they hybridize poorly with one another. That the difference resides in the spacer segment becomes apparent from the denaturation maps, the *X. mulleri* DNA being much more thermally labile over the greater part of this region, and much more resistant in the lesser. Differences in (G+C) content of different parts of the chains are reflected also in absorbance melting curves of the ribosomal DNA of the two species. It thus seems that although extensive homology between the 28 and 18S RNA sequences persists over a great range of disparate eukaryotes, the spacer regions of the precursor are utterly different between two barely

distinguishable species. This is interesting in itself, but more particularly it raises the basic question of how such a mutation in a multiple gene spreads from one copy to another along the chromosome. Brown *et al.* refer to this as horizontal evolution, and uphold the view that some form of scanning and correcting mechanism must operate.

In an accompanying article, Brown and Blackler (*ibid.*, 75) examine the DNA of hybrids of *X. laevis* and *X. mulleri*—which it seems cannot tell the difference. The essential finding is that the paternal multiple genes turn up in the offspring. The inference is that the transmission of these genes occurs by way of at least one copy from the original chromosomal DNA; it eliminates the alternative that the replication involves an independent episomal body—a mechanism which in principle was on the cards, for the amplified ribosomal DNA is packed into nucleoli at the egg cell stage.

Dawid (*ibid.*, 201) has been concerned with the mitochondrial RNA of *X. laevis*. In respect of nucleic acids the mitochondrion operates an independent ecology from the rest of the cell, and has its own characteristic ribosomes as well as DNA. The molecular weight of its DNA is only some 12 million. Dawid finds that the mitochondrial ribosomes and tRNAs hybridize in all with 20 per cent of one DNA strand, corresponding to one of each ribosomal RNA molecule and about fifteen tRNA molecules per DNA. Thus in mitochondria there is—uniquely it seems—no gene amplification. (The curious dearth of tRNA species—apparently not even one per amino-acid, let alone the usual degenerate set of sixty or so—is unexplained. Perhaps the balance are imported from the cytoplasm.)

In a second article, Dawid and Chase (*ibid.*, 217) grapple with the problem of molecular weight determination of the mitochondrial RNA. The ribosomes have been reported to be much smaller than those of bacteria—to which mitochondria are generally likened—and it would not therefore be surprising if the ribosomal RNA were not also small. Melting curves suggest a low degree of pairing, and hence perhaps a relatively expanded structure. This being so, physical measurements, such as sedimentation and electrophoresis on the native molecule, provide, Dawid and Chase assert, a poor estimate of the molecular weight, on the grounds that the species used for calibration are of a different character. By setting up new calibrations in solvents in which base pairing is annihilated, they arrive at molecular weight values which are indeed very low—little more than half of those of the

corresponding *Escherichia coli* species. This article deserves attention outside the field with which it is concerned, for its forthright attempt to meet the perpetual torment of molecular weight determination. Whether it represents the last word (it neglects, for example, to consider variations in partial specific volume) is not yet clear.

On the subject of ribosomal precursors, Kumar and Warner (*ibid.*, 233) have analysed the proteins of the nucleolar particles of HeLa cells, and have found a series of proteins that are not present in the matured ribosomes. Their labelling patterns show them to be long lived, and evidently to remain in the nucleolus after the true ribosomal proteins are expelled, so that they are probably re-used. They are surmised to have some function in the maturation process. Wengler, Wengler and Scherrer (*Europ. J. Biochem.*, **24**, 477; 1972) report that ribonucleoprotein particles, which are of mitochondrial origin, by the criterion of repression by ethidium bromide and not by actinomycin D, turn up in the postmitochondrial cytoplasmic fraction. They suggest that contamination with these species may have misled workers interested in messenger-containing particles emerging from the nucleus. Mirault and Scherrer (*FEBS Lett.*, **20**, 233; 1972) have found a nuclease in the nucleolus of HeLa cells, which is able to break down the 45S nucleolar ribosomal precursor into pieces containing 28 and 18S RNA, as well as some intermediate states. No nucleotides are released, and the enzyme is therefore evidently an endonuclease, which nips the chain in only a few places. It is hoped that this may be a true maturation enzyme.

NEONATES

Lecithin and Respiration

from a Correspondent

ALTHOUGH the mortality rate for premature infants in the first few weeks of life has progressively fallen with greater care and knowledge in their management, many still die of respiratory distress syndrome (RDS)—a disorder in which the lungs do not function normally. Advances in the treatment of RDS are being made but it would obviously be preferable to find ways of preventing its occurrence.

The disorder seems to be due to lack of a surface-active substance produced by cells lining the lungs without which the lungs do not fully expand when the infant is born. Lecithin is thought to be responsible for this surfactant activity and it is known that the lecithin present in the lungs of infants dying of RDS is much less than in those who die from other causes. *In utero* the fluid within the lungs mixes with the

amniotic fluid surrounding the foetus. Recent work by S. G. Bhagwanani, D. Fahmy and A. C. Turnbull of the Welsh National School of Medicine, Cardiff, has shown that it is possible to correlate the quantity of lecithin in the amniotic fluid with the development of RDS and they suggest critical levels below which RDS can be fairly confidently predicted if delivery takes place (*Lancet*, i, 159; 1972).

Although the procedure for the collection of amniotic fluid is not without risks, it is already frequently used in certain cases where the benefits far outweigh any dangers involved, for example, to examine cases where a foetus is at risk from rhesus disease. Under a local anaesthetic a needle is inserted through the mother's abdominal wall into the amniotic sac and a small volume of fluid is withdrawn. Although steps are usually taken to locate the placenta, the needle can penetrate the placenta causing bleeding, and the passage of a needle through the uterine wall can itself stimulate labour, but the incidence of these complications is small.

The Cardiff group discovered, by quantitative assessment of lecithin in amniotic fluid at various times in pregnancy, that lecithin levels rise as pregnancy advances, the rise being most rapid after 32–34 weeks. In 97 infants lecithin levels estimated within twenty-four hours of delivery were 3.5–37.5 mg per 100 ml. and none of these infants developed RDS. Of 13 infants who developed RDS, 12 had lecithin levels of 3.4–0.6 mg per 100 ml. The thirteenth infant who developed very mild RDS had other congenital abnormalities which may have contributed to difficulties in respiration. The lowest lecithin levels were associated with the most severe RDS, and the critical level for lecithin measured twelve to twenty-four hours before delivery appears to be between 3 and 4 mg per 100 ml.

Many infants are born prematurely for reasons which are unknown and cannot be prevented, but many labours are induced before the foetus has reached maturity for maternal reasons or because intrauterine growth is retarded due to inadequacy of the placenta. In such circumstances obstetricians face a real dilemma, and the determination of the moment when the foetus is less at risk of dying once delivered than of dying *in utero* due to placental insufficiency is a difficult problem. It is already possible to measure substances such as oestriol in mothers' urine which give an indication of placental function. If these critical levels of lecithin concentration and their association with RDS are substantiated and the method becomes widely available, it would be a great step forward in neonatal paediatrics.

CANCER RESEARCH

Nature or Nurture?

from a Correspondent

PARTITION of responsibility between nature and nurture in the origin and growth of cancers was the topic of discussion at the fifth meeting in the series on the principles of experimental and clinical oncology at the British Museum (Natural History). The chairman on February 7 was Professor D. G. Harnden (University of Birmingham); the speakers were Dr L. N. Payne (Houghton Poultry Research Station, Huntingdonshire) and Professor J. H. Edwards (Birmingham Maternity Hospital).

Professor Harnden pointed out the formal necessity of distinction between genetic changes in the germ line which lead to heightened susceptibility to cancer and genetic changes in somatic cells such as are involved in the conversion to malignancy. Visible chromosomal changes in malignant cell populations could often be thought of as secondary to the malignant change itself. The exception was the Ph' chromosome which is usually to be found in haematopoietic cells of patients with chronic myelogenous leukaemia. The argument that visible chromosomal difference is likely to be associated with heightened susceptibility to tumours, based on the unusually high incidence of particular tumours in patients with Bloom's syndrome, Down's syndrome and chromatin positive Klinefelter's syndrome, all of which have congenitally abnormal chromosomes, is not supported by a survey of the chromosomes in blood lymphocytes of several thousand patients with an array of cancers. No marked differences are found in the frequency of chromosomal abnormality in people with cancer in comparison with a non-affected control group.

Dr L. N. Payne surveyed experimental studies on the genetic basis of susceptibility. High and low tumour strains of inbred animals have been known for some time, but it was worthy of note that no general susceptibility to cancer had been found but rather predispositions which affected particular tissues or organs. It was always difficult in studies of susceptibility done on whole animals to distinguish between particular environmental influences such as viruses which can be transmitted from parent to offspring and true genetic susceptibility to an extrinsic agent. Studies by Lilly have shown that resistance to the leukaemogenic Gross virus in mice is probably controlled by two pairs of dominant genes. But a polygenic pattern of inheritance of susceptibility is probably more common.

Dr Payne did, however, point out that

much more work with congenic lines of mice was required before the pattern would become clear. Of great interest were the marker genes such as "lethal yellow", "dilute" coat colour and "flexed tail", all of which were associated with high susceptibility to particular tumours. It was not certain whether these were examples of genes with pleiotropic effects or genes closely linked to those which determined susceptibility. Dr Payne's talk indicated very clearly that using either whole animals or their derived fragments in tissue culture it should be possible to understand soon and in detail some of the various mechanisms of susceptibility and resistance to oncogenic influences.

Professor J. H. Edwards, while elated at the array of information concerning genetic predisposition to cancer, was less sanguine about what could be done with it. It was perfectly possible using the techniques of quantitative genetics to establish the heritability of a particular kind of tumour but with only a few rare exceptions the information gained was not useful, principally because there was no marked inheritance of predisposition to the common forms of tumour. In some instances it had proved possible to find associations between particular blood group genes and certain cancers, but the metabolic significance of the finding could not easily be determined. Professor Edwards showed that pedigree studies could be fickle as they tended to change with time if staged on contemporary material.

COSMOLOGY

Gravity and Fred Hoyle

by our Astronomy Correspondent

SIR FRED HOYLE returned to a familiar theme in his presidential address to the Royal Astronomical Society on February 11—the possibility that the local world is not as independent of the large-scale structure of the universe as intuition might lead one to suspect. On the way Sir Fred also delighted the geophysicist fellows of the society with his views on the possible implications of such a cosmology in the history of the Earth. Although Sir Fred would not vouch for the veracity of the particular model which formed the basis of his address, he presented the model as an example of the kind of relationship between the large-scale and the small-scale worlds which is beginning to emerge from cosmological thinking.

This view which has obviously been intriguing Sir Fred recently arises from concepts of the universe in which the origin of the universe is seen not as a true origin but as a discontinuity which he likened to a discontinuity in quantum mechanics. In one such model, the

gravitational constant, G , has to vary in inverse proportion to the time that has elapsed since the origin of the universe, defined in the Friedmann sense. Although Sir Fred admitted that he had always doubted this variability of G , which of course was proposed by Dirac in 1937, he felt that the time was now ripe for a re-examination.

The time variability of G would, for example, have a marked effect on the life-cycles of stars whose speed of evolution at some stages is strongly dependent on G . Larger values of G in the past mean that stars will have evolved faster than is normally supposed from present observations, and this would have many profound implications for astronomy, making the galaxies brighter than they would otherwise be, for example.

Nearer home, Sir Fred talked of the implications for the solar system, bearing in mind that the gravitational constant would have been $4/3$ times its present value at the time of formation of the Earth-Moon system. The luminosity of the Sun would have been something like three times its present value (rather than less bright as used to be suspected) and the Earth would have been nearer the Sun than it is now because the effect of a decreasing value of G is to turn the planetary orbits into steadily expanding spirals. Sir Fred speculated on what the meteorological conditions might have been like at the time of formation of life on the Earth, possibly 3×10^9 years ago, and suggested that the gradual cooling of the terrestrial atmosphere and surface as G decreased and the Sun became less bright and further away might have been a factor controlling the type of life that could evolve.

Turning to geophysics, Sir Fred confessed to being happy with the kinematics but not the dynamics of continental drift. He suggested that a world-wide cracking of the surface to form the rigid plates, as the Earth expanded due to the changing value of G , might be a way out of the difficulty, and he speculated that similar processes may have to be taken into account on other planets, notably Jupiter.

NERVE

Receptors in Axons

from our Neurochemistry Correspondent
A REPORT by J. L. Denburg, M. E. Eldefrawi and R. D. O'Brien, of Cornell University, in a recent issue of the *Proceedings of the US National Academy of Sciences* (69, 177; 1972), which shows the presence, inside nerve axon membranes, of a macromolecule with many of the properties of the receptor for acetylcholine, promises to be of great interest, because it suggests

that previous theories of axonal conduction may be incomplete.

Conduction of impulses along nerve fibres occurs by the propagation of brief electrical signals, termed "action potentials". According to the membrane concept, built up in the past thirty-five years, action potentials arise from a sudden change in the polarity of the cell membrane caused by a breakdown in its selective permeability to certain ions. A potential difference normally exists across the axon membrane, because its permeability to potassium and chloride ions is much greater than to sodium ions. Stimulation, however, causes the membrane to become leaky to sodium ions, and as a result a sudden influx of sodium ions occurs and the potential of the membrane is rapidly reversed. The phase of sodium entry is transitory, and is followed within 1 or 2 milliseconds by an outward movement of potassium ions, which tends to return the membrane potential to its initial level, and hence restore the original selective permeability of the membrane such that it is once more excitable. Because nerve fibres are to a certain extent like conducting cables, an impulse at a particular point spreads to adjacent parts of the fibre, and this in turn causes a regenerative entry of sodium ions, leading to a full-sized action potential. Thus impulses are propagated in an all-or-none fashion along the fibre.

By contrast, transmission of impulses across synapses, at the terminals of nerve fibres, is believed to occur by the release of certain chemical transmitters, which diffuse across the synaptic cleft and interact with specific receptors on the postsynaptic membrane. At the mammalian neuromuscular junction, interaction of the transmitter, acetylcholine, with receptors on the muscle surface causes an indiscriminate increase in cation permeability, thereby reducing the membrane potential to zero and triggering muscle action potentials.

Sensitivity to acetylcholine is normally restricted to junctional regions, but Nachmansohn has shown that impulses in nerve and muscle are blocked in the presence of large doses of inhibitors of cholinesterase, the enzyme which destroys acetylcholine. He has suggested that a local release of acetylcholine, similar to that occurring at nerve endings, is responsible for the excitation of axon membranes and its underlying permeability changes. Drugs such as curare, which is a competitive antagonist to acetylcholine at end-plate receptors, do not, however, affect axon conduction, and other drugs, such as tetrodotoxin and tetraethyl ammonium, which block axon conduction by specifically interfering with the sodium and potassium channels in nerve, have no effect on the sensitivity of end-plate receptors to applied

acetylcholine, and this has led to severe criticism of Nachmansohn's theory.

The possibility that certain drugs act specifically at ACh receptors, together with a potentially good source of postsynaptic membranes rich in such receptors in the electric organs of certain fish, has stimulated a tremendous surge of interest recently in methods for the isolation and characterization of the cholinergic receptor. O'Brien and his colleagues have themselves used the technique of reversible equilibrium dialysis to study the binding of cholinergic drugs to a particulate fraction from the *Torpedo* electric organ, and in the present experiments they extend these methods to use on preparations of axon plasma membrane from lobster nerves.

Denburg *et al.* found that the membrane preparation bound labelled nicotine, a known cholinergic ligand, with a K_D of $0.42 \mu\text{M}$, indicating a reasonable affinity. Even in the presence of a high concentration of a cholinesterase inhibitor, binding of ^3H -acetylcholine could not be detected, but acetylcholine inhibited the binding of nicotine with a K_i of $43 \mu\text{M}$, suggesting a relatively low affinity. The binding of nicotine was also inhibited by several other drugs known to act as cholinergic receptors, including α -bungarotoxin, but was unaffected by non-cholinergic drugs. Furthermore, it was found that the local anaesthetic, procaine, which blocks axon conduction by interfering with both sodium and potassium channels in some way as yet unknown, also depressed nicotine binding.

The presence, in axon membranes, of a component capable of binding cholinergic agents suggests that Nachmansohn's theory needs to be reconsidered. It has, however, not been proved that binding of agonist to the "receptor" macromolecule is a necessary element in conduction—axons perfused with simple saline solutions are capable of conducting impulses for several hours. O'Brien and his colleagues quote evidence that curare, injected inside axons, blocks conduction, but this is only in concentrations of 1 to 10 mM. Similarly, the inhibition of nicotine binding by procaine observed in the present experiments is not sensitive to the concentration of calcium, as is the effect of procaine on conduction, which suggests that the two effects may be independent.

Preliminary indications are that the nicotine-binding site is a phospholipoprotein molecule. It is possible that large molecules of this sort are a necessary structural component of all membranes and, although they remain on the inside of the membrane at indifferent sites, at the highly specialized junctional sites to which sensitivity to acetylcholine is normally restricted, they are mobilized to the outside of the membrane.

Ducks, Drakes and Barrages

NEXT week should see the publication of the Water Resources Board's full feasibility study of the Morecambe Bay scheme. The intention is to supply 500 million gallons of water a day from off shore reservoirs and barrages to help meet the growing demand for water. The study is expected to outline possible methods and recommend which scheme be adopted, depending where the government decides its priorities lie—in simply supplying water cheaply or in taking advantage of such possible side benefits as a link road across the top of the barrages to Barrow-in-Furness. But the Morecambe Bay scheme is only one of the three estuary schemes under study at the moment.

England and Wales use 14,000 million imperial gallons (65×10^9 l.) of water a day, and the demand is rising. Already the average domestic consumption per head is 38 gallons a day, but industry uses six times as much—it takes 200 tons of water to make one ton of steel, for example. By the year 2000 consumption will probably be about 30,000 million gallons a day.

So far, reservoirs, natural and artificial, above and below ground, have met the need. But by the end of the century new sources will be needed, even if industry learns to use water more sparingly. The Water Resources Board cheerfully expects that the re-use of water within factories may stabilize the industrial demand, but other demands will grow. Possible new sources are groundwater schemes, desalination, more reservoirs, more sewage recycling—and estuary storage schemes.

The idea behind estuarial schemes is essentially that a barrage is thrown across an estuary to store fresh water, or pumped fresh water storage reservoirs are built within the estuary. The idea of building barrages to store water or to reclaim land is not new. Sir John Rennie, the nineteenth century engineer, proposed schemes for the estuaries of the Humber, Forth, Tay, Clyde, Solway and Mersey, and at Morecambe Bay and the Wash. But only in the past decade have estuary schemes had a real chance of being built.

Consideration of estuary schemes is, however, complicated by a multiplicity of factors. Estuaries large enough to make water storage economic usually have towns near their heads and wildlife near their mouths. The effects—beneficial or otherwise—that a barrage will have on communication, recreation, ecology, fishing industries, land drainage and reclamation, industrial and urban development and local

scenery have to be considered, apart from establishing whether the scheme will provide an economic supply of water. The lines of battle over estuary schemes tend to be drawn up with the conservationists and fishing industries opposed to the scheme, the National Farmers Union cautiously in favour—estuary schemes mean fewer farms flooded for inland reservoirs, better local drainage and the possibility of

land reclamation—and the local industry standing wherever it sees most gain, with the Water Resources Board, which is responsible for investigating the schemes, maintaining a precarious neutrality and refusing to prejudge the issue.

Morecambe Bay

The first scheme for Morecambe Bay was put forward by George Stephenson

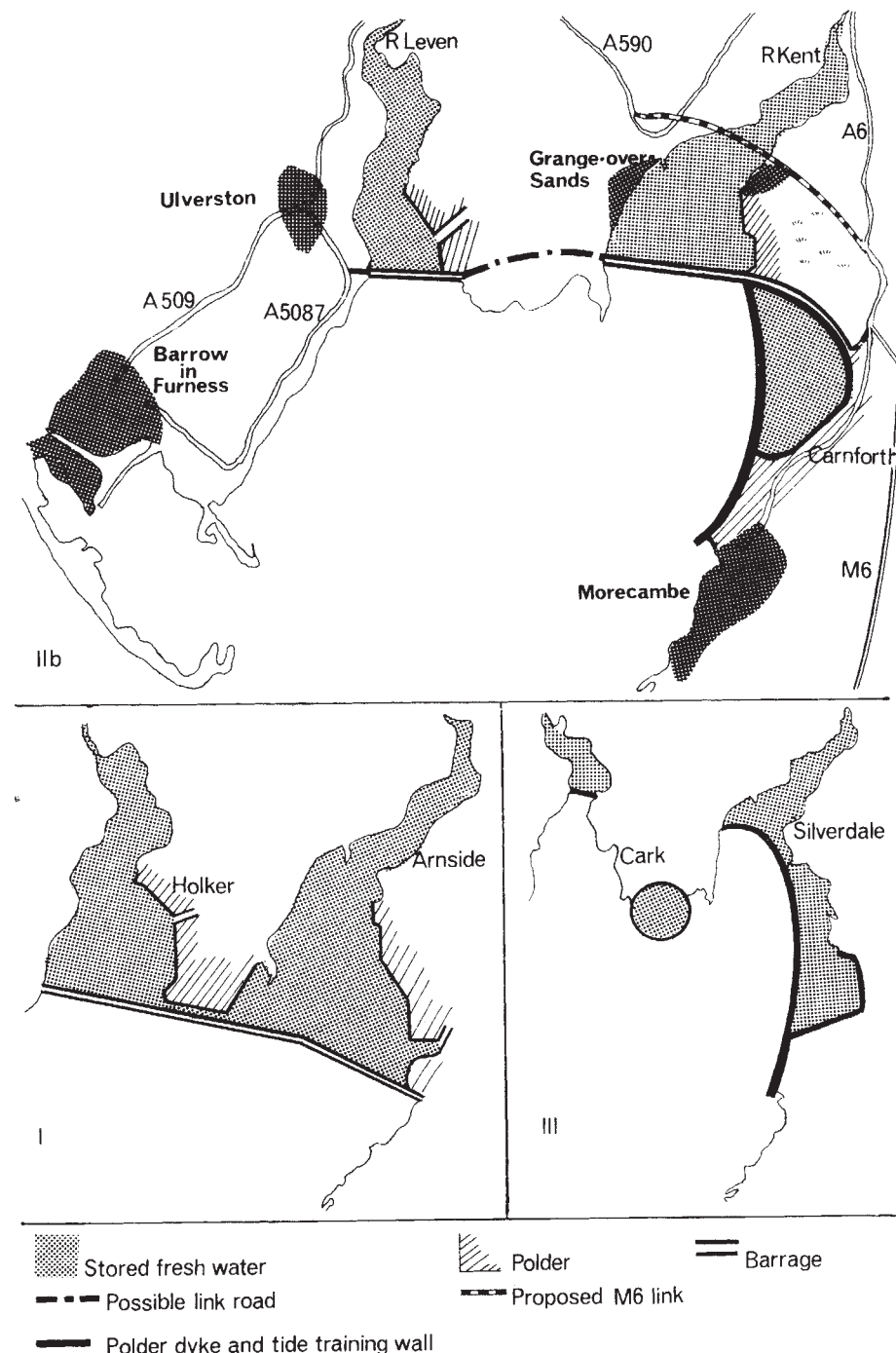


Fig. 1 Three of the proposed schemes for Morecambe Bay. Scheme IIa is similar to IIb save that a reservoir, polder area and tide training wall stretch down to Morecambe as in scheme III, and there is no reservoir off Carnk.

in 1837. He wanted to run an embankment and railway line across the bay, but his £0.5 million plan was rejected by Parliament in 1840 as being too expensive. Other proposals made this century did not receive much support until Leonard Leeming, surveyor to Urmston District Council, proposed an 11.5 mile full barrage running east to west across the bay in 1964. In 1965 the Water Resources Board ran a desk study on the scheme and also on a proposed scheme for the Solway Firth, which has since been dropped due to the cost of water transmission. The desk study recommended the full study which once published will be discussed by the plethora of interested bodies.

Provision of water is the central consideration at Morecambe Bay. Although there are other potential benefits in recreation, communication and land drainage, these are secondary to the need to supply 500 million gallons a day. Although the study has yet to be published it is apparent that the original scheme for a full barrage has fallen from favour on the grounds of cost and damage to the environment. Although seven other schemes are included in the study, the most likely candidates are three which have already been made public, known as IIa, IIb and III (see Fig. 1). These involve putting barriers or half barriers across the rivers Kent and Leven and storing the water in banded reservoirs off shore. Siltation could be a problem with all the schemes, although less so with scheme III, which could affect the ports of Barrow, Heysham and Fleetwood. Siltation could be overcome by dredging, but would add to the running cost of the scheme. The considerable fringe benefits include the possibility of a road link to Barrow-in-Furness, which it is estimated

would save Britain £18 million a year, improved land drainage and much improved recreational facilities for the resort of Morecambe, including fresh water nature reserves and possibilities for a marina. Scheme III offers little benefit to Barrow as a road is not included in the plans. This may be offset by a separately proposed link road to the M6 over the Kent estuary. In contrast, scheme IIa will have little benefit for Morecambe, as it does not include a tide training wall.

The discussion of these schemes has produced violent differences of opinion in the areas they affect. In Barrow and Morecambe there is great enthusiasm provided each derives the benefits they expect, but in Arnside there has been considerable opposition in the form of the well organized Morecambe Bay Society. Its objections are that the proposed schemes will all be eyesores to a greater or lesser extent—the barrages would be 15 foot above high water, and the walls of the reservoirs between 20 and 40 foot—and they will damage the local ecology. Certainly the local fishing industries are likely to suffer, but considerable freshwater habitats could be built up. The society also argues that once the tidal influence has been removed from the bay there will be considerable weed growth leading to rotting and stinking vegetation when the water levels are low. The society's attitude, however, is not all negative. It has also proposed an alternative scheme, pumping water through underground aqueducts from high up the Leven, Crake and Kent rivers to two reservoirs built on marshland off the coast at Cark and between Carnforth and Silverdale. The Water Resources Board has considered this proposal seriously, and the findings will be in-

cluded in next week's report, but it is believed that the scheme would cost rather more than the barrage schemes and yield rather less water—a price that the Morecambe Bay Society thinks is worth paying, but it remains to be seen whether the Water Resources Board will agree.

The Dee Scheme

The second scheme under consideration is the Dee estuary scheme. Of the three schemes it is the one most likely to go ahead. It is essentially a road scheme with water storage very much taking the back seat. A full feasibility study of the proposed scheme was published in March 1971 by Binnie and Partners since when interested bodies have commented on the report to the Department of the Environment but no decision has yet been announced. The River Dee rises in Merioneth and runs into the Irish Sea through a broad but shallow estuary, one side of which is in Cheshire and the other in Flintshire. The consultants reported that there was a strong case for a multipurpose scheme for the Dee estuary centred around a road crossing with pumped storage reservoirs situated in the neck of the estuary. The joint schemes would give improved communications leading to considerable urban and industrial growth, particularly on the Flint side of the estuary, giving a population of 280,000 by the year 2000 with 16,000 people commuting daily to Lancashire and Cheshire. Freer access to North Wales would become available and recreational facilities would be improved. The consultants recommend three road crossing schemes but plump for a Flint-Burton crossing with a coast road (see Fig. 2). For water conservation deeper reservoirs in the neck of the estuary giving a contracted estuary shape are preferred to shallower but more extensive works stretching much further downstream. The walls would be between 10 and 20 metres high and the reservoir could eventually yield up to 250 million gallons a day.

The Dee estuary, particularly towards its mouth, is rich in wildlife, and the Nature Conservancy urges in an appendix to the main report that a contracted estuary shape should be used if water storage has to be adopted. Any storage scheme will affect the salt water habitats, but will also carry benefits in the creation of new freshwater habitats. Considerable recreation facilities would become available, as well as some reclaimed land, although, apart from some land for grazing, this would be of more use to industry than to agriculture. The cost of the various schemes, which would be built in stages over several years, ranges between £65 and £78 million. There are, however, two complicating factors in the form of

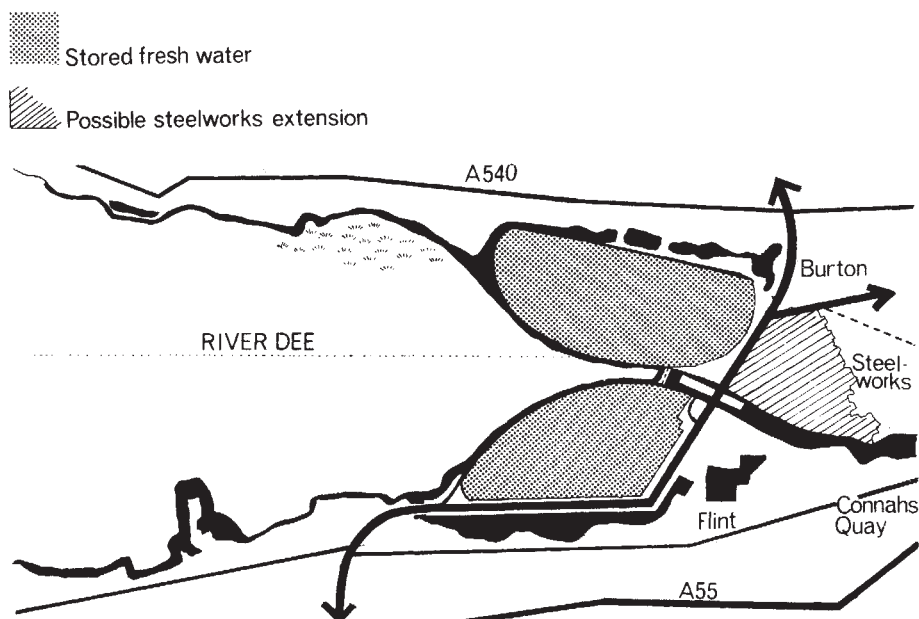


Fig. 2 One of the possible schemes for the Dee estuary.

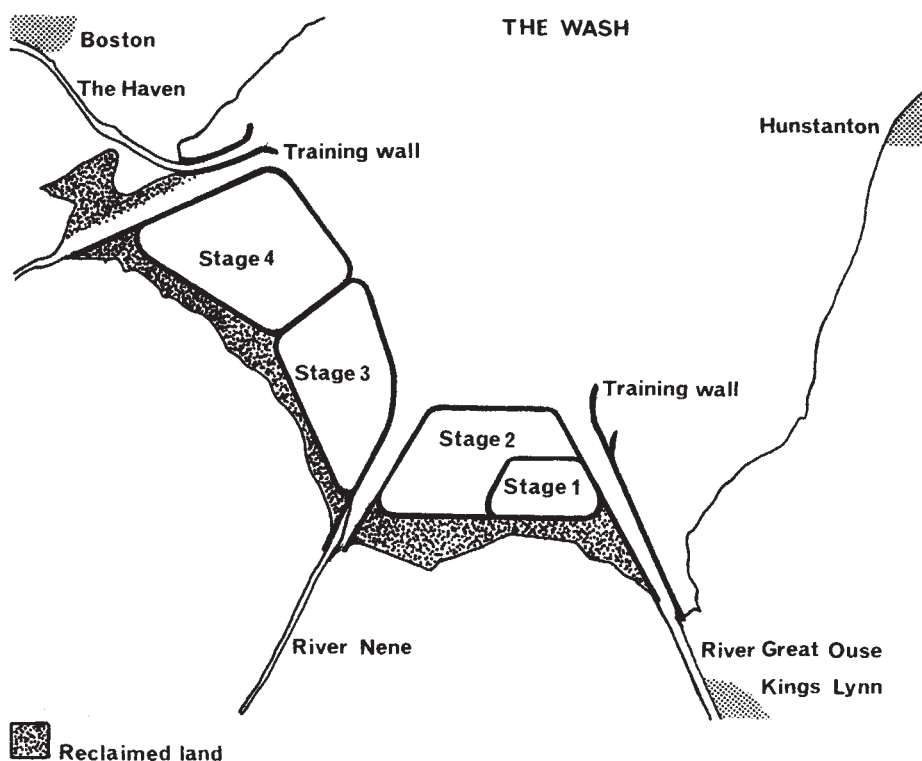


Fig. 3. The proposed Wash scheme. Only the stage 1 reservoir is needed this century.

proposals to build a nuclear power station at Connaught's Quay and to extend the steelworks at Shotton.

The consultants warn that plans for the 1,250 MW nuclear power station, first announced in 1969, are incompatible with their plans for major urban growth in the area. As well as the problems associated with having a nuclear reactor near residential areas there are difficulties over the proposed cooling system for the power station. To build special cooling ponds would intrude upon the proposed estuary schemes and increase water costs by up to 15 per cent, so cooling towers would have to be built. The CEBG seems to have accepted this, but a power station would still limit urban growth. A public inquiry was held in March 1971, but the outcome has not yet been announced.

The British Steel Corporation's application in 1970 to extend the strip steel mill at Shotton, popular though it might be with the local labour force, could increase the cost of the barrage schemes by as much as £3 million or £4 million. At present the BSC does not have the money to afford the expansion, but the steel mill remains a potential spanner in the works.

But whatever the decisions on Connaught's Quay and Shotton, the full report on the scheme is now with the Welsh Office and the Department of the Environment and all now waits on their decision.

The Wash

The third major estuary scheme under consideration is the plan for the Wash, which is still in its comparative infancy. Schemes to dam or reclaim the Wash have been produced during the past century with regularity and varying degrees of ambition ranging from a little land reclamation to the construction of a Europort taking up most of the Wash and including water conservation, land reclamation and a complete new city. Some of the more ambitious plans were put in their place by a desk study of estuary storage in the Wash, the results of which were published in 1970, which concluded that with present technology it would not be possible to build a barrage right across the mouth of the Wash. To build one further in towards the land would be unnecessary as more efficient and economical water supplies are available from banded reservoirs. The desk study recommended that a full feasibility study be undertaken on four staged storage reservoirs, and work on this £2.6 million study began in June 1971. The study is being staged so that a decision can be taken in 1973-4 whether to build the number one reservoir (see Fig. 3) by 1983-4 to give a yield of 100 million gallons a day at a total cost of £25 million. The walls of the reservoirs would be 9 metres above sea level. Only the first stage reservoir would be needed this century, but if the full plan is implemented the four reservoirs will

give a yield of 530 million gallons a day at a total cost of £140 million. At a recent meeting in King's Lynn to discuss the proposals, there seemed to be remarkably little opposition to the scheme (see *Nature*, 235, 351; 1972). The local fishermen feel themselves threatened, and there are fears locally that the tides will prove too strong. But by and large the advantages of the scheme—a large supply of fresh water, some reclaimed land, new freshwater habitats and recreational facilities, not to mention the possibility of the scheme paying for itself by the discovery of King John's treasure—seem to outweigh the possible disadvantages.

But, at best, the estuary schemes under consideration can only meet part of the demand. There are bound to be more reservoirs, more sewage recycling and greater re-use of water. But more reservoirs mean more valleys drowned and stronger protests from the environmentalists; and again, reservoirs cannot be easily built in the densely populated and relatively flat south of England.

Groundwater schemes offer considerable possibilities in certain areas and are already in operation in Lambourn valley and the Great Ouse area. Water is pumped out of the aquifer in times of drought and pumped in, for storage, in times of plenty. First tests have shown that underground storage should be possible and economic, and studies are being made on the chalk areas of the south-east and on areas with Triassic sandstones. But yield from groundwater schemes on the scale of the Great Ouse and Thames areas (the latter is expected to produce 100 m.g.d. by 1981) cannot be expected in the North or Wales and the Midlands.

Desalination is unlikely to make a major contribution this century, according to the Water Resources Board, and the recent problems with freeze desalination plant at Ipswich have not brought commercial desalination any nearer.

Given the large yields and attendant benefits estuary schemes offer, they could play a considerable part in meeting future demands, provided the damage they cause is not too great. No decision has yet been taken on any of the above schemes, however, and none will be until the publication of the Water Resources Board's report on the future of water supplies in England and Wales in late 1972 or early 1973. This report will be the culmination of a five-year survey of the likely future needs of the two countries. Once the future needs and potential sources are known and have been costed against water from estuary schemes which tend to give larger supplies per day than reservoirs, then decisions can be made on whether or not to build the estuary schemes with all their attendant benefits and disadvantages.

Targets of Penicillin Action in *Escherichia coli*

RAINER HARTMANN, JOACHIM-VOLKER HÖLTJE & ULI SCHWARZ

Friedrich-Miescher-Laboratorium der Max-Planck-Gesellschaft, Tübingen

Evidence is presented that the physiological effects of penicillin on *E. coli* may be due to interaction with at least two specific targets, both of which are enzymes.

PENICILLIN has been shown to interfere with the biosynthesis of the structural element of the bacterial cell wall^{1,2}, the

sacculus³. The antibiotic was thought to inhibit one enzyme involved in the production of the sacculus^{4,5}. Biochemical and morphological studies have led us, however, to suggest that, at least in *Escherichia coli*, there is more than one target for penicillin action⁶. This article deals with the characterization and initial purification of two penicillin-sensitive enzymes from *E. coli*. It is considered that the physiological effects of penicillin action are due to an inhibition of these enzymes.

Both enzymes accept as a substrate the polymer murein which forms the sacculus. The murein is a net-like assembly

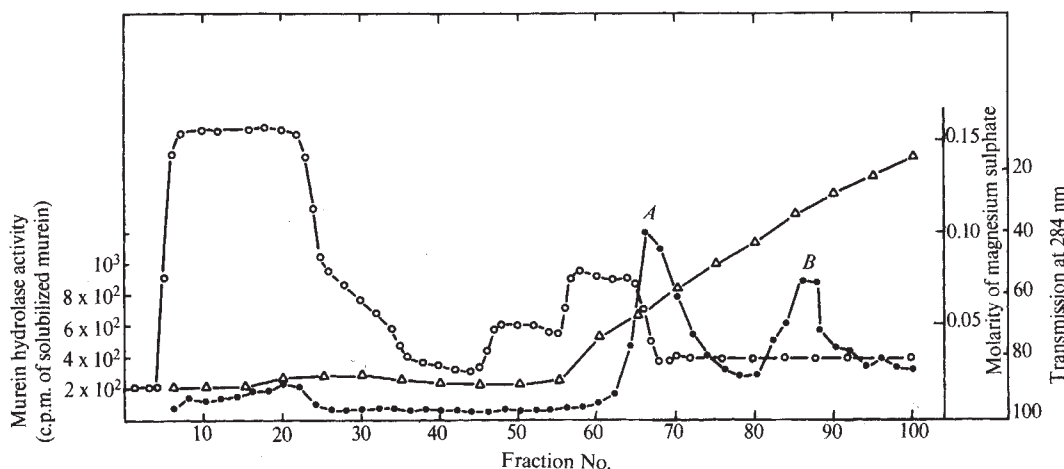


Fig. 1 Chromatography of murein hydrolases from a cell envelope fraction. Cell extracts were made from *E. coli* W7 throughout. Strain W7, requiring both DAP* and lysine, lacking DAP-decarboxylase¹⁶ is a derivative from strain W 173-25 (ref. 17). 14 g dry weight of cells, grown in minimal medium¹⁸ (5×10^8 cells/ml.) were opened in an 'X-press' (Biox AB, Nacka, Sweden) after one wash with 0.01 M Tris-maleate (pH 6.8). After sedimentation (20 min at 48,000g), the envelope sediment was washed once with 0.01 M Tris-maleate (pH 7.2), 10^{-2} M EDTA, and twice with 0.01 M Tris-maleate (pH 6.8). Murein hydrolases were extracted with 80 ml. of 2% 'Triton X-100', 0.5 M NaCl, 0.01 M Tris-maleate (pH 6.6) for 20 min at room temperature. The solubilized enzymes were separated from the envelopes by centrifugation (30 min at 28,000g) and dialysed overnight against 0.01 M Tris-maleate (pH 5.2), 10^{-2} M magnesium sulphate. After discarding precipitable protein, the envelope extract was applied on a CM-cellulose column (2.5–40 cm). The column was eluted with a linearly increasing salt-pH-gradient (250 ml. 0.01 M Tris-maleate (pH 5.2), 0.025 M magnesium sulphate; 250 ml. 0.01 M Tris-maleate (pH 6.2), 0.25 M magnesium sulphate), at a flow rate of 24 ml./h; fraction volume was 4.8 ml. Assay for murein hydrolase activity: 20 μ l. of the fractions were added to 160 μ l. 0.01 M Tris-maleate (pH 6.8) with 0.2% 'Triton X-100', 5×10^{-3} M magnesium sulphate, 0.2% bovine serum albumin. As a substrate 20 μ l. of 3 H-DAP-labelled sacculus suspension: (see below) was added. After 1 h of incubation at 37° C, the reaction was stopped in ice by addition of 20 μ l. of 50% trichloroacetic acid and 20 μ l. of 5% bovine serum albumin in water. The compact precipitate was pelleted for 5 min at 12,000g. From the supernatant 100 μ l. were neutralized with 0.5 ml. of 0.1 N sodium hydroxide and added to 5 ml. of scintillation liquid to be counted in a homogeneous phase. Labelled sacculi were obtained from *E. coli* W7 grown with 1.5 μ g/ml. of 3 H-DAP (Radiochemical Centre, Amersham; 70 mCi/mol) as described¹⁹. The final substrate suspension was obtained by mixing labelled sacculi with unlabelled material (2×10^6 c.p.m./mg; 0.44 mg sacculi/ml. of suspension, estimated by chemical determination of DAP content)²⁰. ●, Murein hydrolase activity in fractions; ○, transmission of eluate at 284 nm; △, molarity of magnesium sulphate in eluate.

* DAP, 2,6-diaminopimelic acid.

of polysaccharide strands which are interlinked by short peptide bridges. The enlargement of the murein net might be expected to require two sets of enzyme activities. The sacculus is a closed structure which probably is enlarged by specific cleavage of murein, with the addition of new building blocks into the growing point in a second step⁷. The morphological modifications of a sacculus during cell growth, therefore, can be accomplished only when the murein degrading enzymes—murein hydrolases—provide acceptor sites for incoming new material at the right place, at the right time, and in the right order and amount. This makes them key enzymes in murein biosynthesis and, thus, in bacterial morphogenesis. We present evidence that penicillin blocks the activity of two murein hydrolases from *E. coli*.

Murein Hydrolases

Degradation of high molecular weight sacculi into small reaction products is used to assay murein hydrolase activity. We have developed a sensitive assay system, using as a substrate radioactively labelled sacculi with covalently linked lipoprotein which makes them precipitable with trichloroacetic acid (Fig. 1).

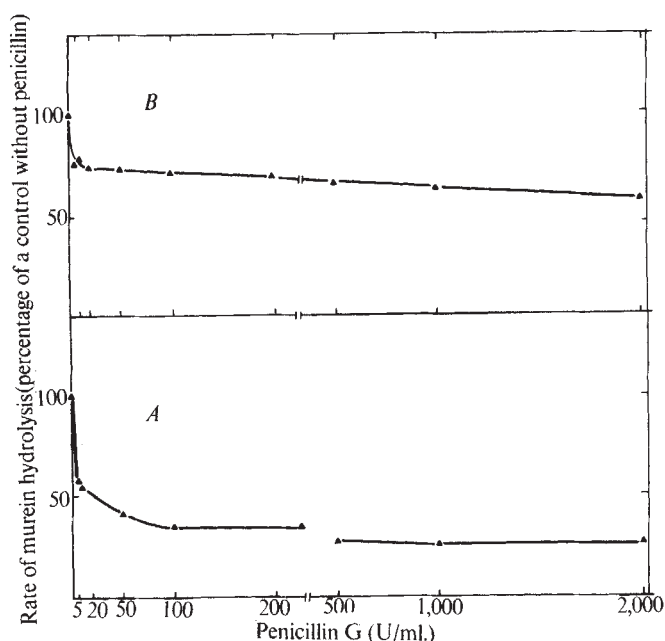


Fig. 2 Penicillin sensitivity of hydrolases after solubilization from cell envelopes. *A*, Purified enzyme, pooled fractions from peak *B* (Fig. 1), concentrated to 6.8 ml. by ultrafiltration (Diaflo; membrane PM 10). To the assay mixture (Fig. 1; serum albumin omitted), 30 μ l. of enzyme solution (3.3 μ g of protein) were added together with penicillin G to give the final concentrations indicated on the abscissa. Total volume of samples was 200 μ l. the assay procedure as described (Fig. 1). *B*, Crude enzyme preparation from 'Triton'-treated envelopes (Fig. 1). Assay procedure as above except that 10 μ l. of the enzyme preparation were assayed. Enzyme from peak *A* (Fig. 1) was not inhibited by penicillin up to 500 U/ml.; 1,000 U/ml. reduced enzymatic activity only to 90% of a control.

Murein hydrolase activity detected in the cell envelope sediment and in the supernatant fraction after disintegration of *E. coli* cells, is stimulated by magnesium ions at an optimal concentration of 10^{-2} M.

Some hydrolases are strongly bound to the envelope fraction and cannot be washed off with buffer. A 30 min incubation with 'Triton X-100' and sodium chloride, however, solubilizes 50% of the total hydrolase activity in the cell envelope. The solubilized enzymes can then be fractionated on a CM-cellulose column. A small amount of hydrolase activity is not absorbed

onto the column, and that which is separates into two peaks, *A* and *B* (Fig. 1). The activity of peak *B* is inhibited by penicillin whereas that of the other fractions is not.

Peak *B* enzyme converts the dimer murein subunit C3 into monomer C6^{3,8} by hydrolysis of the bond which interlinks peptide side chains in the murein which bridge adjacent polysaccharide chains³. Thus the enzyme is an endopeptidase.

The inhibition of endopeptidase activity by penicillin is shown in Fig. 2*A*. The purified enzyme is much more sensitive to penicillin than the activity in the crude extract (Fig. 2*B*). There are two explanations for this finding. First, the crude extract contains enzymes which are not inhibited by penicillin (Fig. 1) but which are detected in our assay. Second, penicillin interacts unspecifically with proteins^{9,10} which make up the bulk of the crude enzyme preparation. This is substantiated by the observation that with the addition of 1.25 mg/ml. of serum albumin the effect of 50 U/ml. of penicillin on pure enzyme is reduced to 16% of a control.

After sedimentation of the cell envelopes, total enzymatic activity in the supernatant has a sharp optimum at pH 4.5 and a second broad optimum at pH 7. An enzyme with pH optimum at 4.5 is penicillin sensitive.

Hydrolases from the supernatant can be fractionated after several purification steps by chromatography on a DEAE-'Sephadex' column (Fig. 3). The enzyme in peak *D* is penicillin sensitive and as it is very labile, its activity can only be assayed when serum albumin is added as a stabilizer. For this reason inactivation curves with purified enzyme are not yet available. As penicillin interacts unspecifically with proteins, the inhibitory effect of penicillin on the pure enzyme may be significantly higher than that shown in Fig. 4.

Peak *D* enzyme is a glycosidase and its main reaction product is a disaccharide with an attached murein-specific peptide side chain. Extensive chemical analyses, which will be published later, indicate that the amino-sugars in this product are carbon 1-1 linked to give a trehalose-like structure with no reducing sugar end-group.

Function of Sensitive Enzymes

Amino-sugar dimers similar to the glycosidase reaction products are found in small amounts in lysozyme digests of *E. coli* sacculi⁸. It is assumed that these are the ends of the polysaccharide chains at which chain growth commences during murein biosynthesis, and this would explain our failure to find reducing sugar end-groups in murein from *E. coli*. We conclude that the glycosidase creates these polysaccharide chain initiation groups in a growing sacculus.

Even though both endopeptidase and glycosidase are assayed as hydrolases, these enzymes might also function as transferases which catalyse a two step reaction. In this scheme, step one would be the hydrolysis of murein and step two a subsequent insertion of new building blocks. The peak *B* endopeptidase may be identical to the transpeptidase activity previously described in a particulate fraction from *E. coli*¹¹⁻¹³. The transferase character of this enzyme has been demonstrated and it is assumed that this enzyme catalyses peptide bridge formation during murein biosynthesis^{11,12}. Transferase characteristics for the glycosidase are indicated in the transfer of free N-acetyl-glucosamine into a disaccharide. A more extensive report of the characteristics of this enzyme will be published.

If indeed the murein hydrolases can be considered to function as transferases, the generally held concept of an interplay between two sets of enzyme activities in murein biosynthesis has to be revised for at least two steps in this complex reaction sequence.

Mechanism of Penicillin Action

There is a structural similarity between penicillin and part of the endopeptidase-substrate of the murein precursor. This

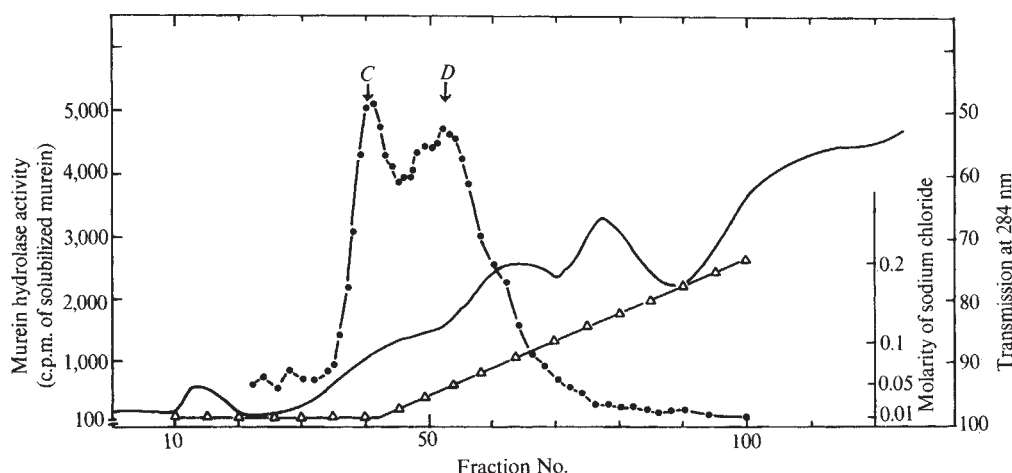


Fig. 3 Purification of murein hydrolases from the supernatant by DEAE-'Sephadex' chromatography. Cells from W7 (Fig. 1); 12 g dry weight, were resuspended in 80 ml. of distilled water after one washing with water. After mechanical disintegration and centrifugation (Fig. 1), the supernatant was fractionated with ammonium sulphate precipitation. The precipitate after 30% saturation was discarded, the precipitate after 50% saturation showed hydrolase activity. It was dissolved in 2 ml. 10^{-2} M sodium phosphate (pH 6.8), 10^{-3} M mercaptoethanol, applied to an 'Agarose' column ('Bio-Gel' A-1.5 m; 100–200 mesh; 2.5 cm $\times$ 96 cm) and eluted with phosphate buffer as used above (15 ml./h; fractions 2.5 ml.). Hydrolase activity was eluted in a broad double peak 75 ml. after the exclusion volume in a total of 150 ml.; it was concentrated to 35 ml. by ultrafiltration (Fig. 2) and applied to a DEAE-'Sephadex' column (2.5 cm $\times$ 36 cm), equilibrated with phosphate buffer. Enzyme was eluted with a linearly increasing sodium chloride gradient (250 ml. 10^{-2} sodium phosphate (pH 6.8), 10^{-3} mercaptoethanol, 0.05 M sodium chloride; 250 ml. of same buffer, 1 M sodium chloride). Elution time was 18 ml./h; fractions of 3 ml. were collected in vials containing 50 μ l. of 2.5% bovine serum albumin as a stabilizer. Hydrolase activity of the fractions: 25 μ l. of each fraction, 25 μ l. of substrate suspension (Fig. 1) and 150 μ l. 10^{-3} M sodium acetate (pH 4.5), 10^{-2} M magnesium sulphate, were incubated for 3 h at 37° C. Further processing was as described (Fig. 1). Enzyme activity from peak D was reduced to 60% of a control by 2,500 U/ml. of penicillin G whereas activity from peak C remained unaffected. ●, Murein hydrolase activity in fractions; —, transmission of eluate at 284 nm; Δ, molarity of sodium chloride in eluate.

similarity caused the assumption that penicillin acts by competing with the endopeptidase for substrate, and thus blocking its activity⁵. Though the question is still open, this interpretation might well explain, at least in part, the biological effect of the antibiotic. In addition we can also demonstrate the inhibition of a second murein specific enzyme by penicillin. This enzyme, a glycosidase, acts on the polysaccharide chains of murein, which can also be visualized as a structural analogue of part of the penicillin molecule¹⁴. When glycosidase activity is specifically blocked it might be expected that the number of starting groups for polysaccharide chain synthesis would be reduced. As a consequence, the overall rate of murein synthesis would be decreased. This is exactly what is observed² although until now unexplained in molecular terms.

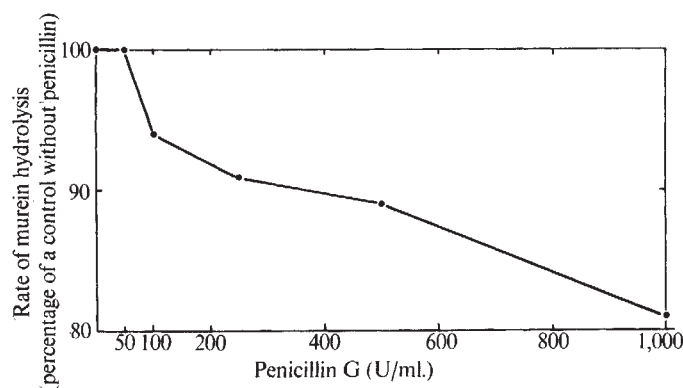


Fig. 4 Penicillin sensitivity of supernatant enzyme. Hydrolase activity of the unfractionated supernatant was assayed (Fig. 3; before ammonium sulphate-step). Penicillin G was added to the samples to give the final concentrations as indicated on the abscissa. Total sample volume was 200 μ l. Means from three independent determinations are plotted.

Penicillin has two distinct morphological effects in *E. coli*. Cell division is blocked at a concentration higher than 20 U/ml.^{6,15} whereas cell elongation is increasingly affected only at concentrations which are higher than 100 U/ml. The concentrations of penicillin which stop cell division and which block endopeptidase activity are about the same⁶. The concentrations which affect cell elongation and glycosidase activity in the crude cell extract are of the same order of magnitude. Based on these observations we favour the hypothesis that there are at least two physiological targets for penicillin action in *E. coli* which together are responsible for its antibiotic effects. The endopeptidase would be predominantly involved in the process of cell division and the glycosidase in cell elongation. Our *in vitro* studies may not, however, necessarily reflect the situation *in vivo*, tempting though the speculation may be. Conditional penicillin resistant mutants with defective murein hydrolases would greatly assist in elucidating the action mechanism of penicillin and the morphogenetic function of the murein hydrolases. From our data one would expect to find at least two complementary types of such mutants.

Received May 28, 1971.

- ¹ Strominger, J. L., Izaki, K., Matsushashi, M., and Tipper, D. J., *Fed. Proc.*, **26**, 9 (1967).
- ² Rogers, H. J., *Bact. Rev.*, **34**, 194 (1970).
- ³ Weidel, W., and Pelzer, H., *Adv. Enzymology*, **26**, 193 (1964).
- ⁴ Wise, E. M., and Park, J. T., *Proc. US Nat. Acad. Sci.*, **54**, 75 (1965).
- ⁵ Tipper, D. J., and Strominger, J. L., *Proc. US Nat. Acad. Sci.*, **54**, 1133 (1965).
- ⁶ Schwarz, U., Asmus, A., and Frank, H., *J. Mol. Biol.*, **41**, 419 (1969).
- ⁷ Shockman, G. D., *Bact. Rev.*, **29**, 345 (1965).
- ⁸ Primosigh, H., Pelzer, H., Maass, D., and Weidel, W., *Biochim. Biophys. Acta*, **46**, 68 (1961).
- ⁹ Lawrence, P. J., and Strominger, J. L., *J. Biol. Chem.*, **245**, 3653 (1970).
- ¹⁰ Batchelor, F. R., Dewdney, J. M., and Gazzard, D., *Nature*, **206**, 362 (1965).

- ¹¹ Izaki, K., Matsuhashi, M., and Strominger, J. L., *J. Biol. Chem.*, **243**, 3180 (1968).
¹² Araki, Y., Shimada, A., and Ito, E., *Biochem. Biophys. Res. Commun.*, **23**, 518 (1966).
¹³ Leyh-Bouille, M., Ghuyssen, J.-M., Bonaly, R., Nieto, M., Perkins, H. R., Schleifer, K. H., and Kandler, O., *Biochemistry*, **9**, 2961 (1970).
¹⁴ Collins, J. F., and Richmond, M. H., *Nature*, **195**, 142 (1962).
¹⁵ Starka, J., and Moravova, J., *Folia Microbiol.*, **12**, 240 (1967).
¹⁶ Davis, B. D., *Nature*, **169**, 534 (1952).
¹⁷ Hoare, D. S., and Work, E., *Biochem. J.*, **61**, 562 (1955).
¹⁸ Vogel, H. J., and Bonner, D. M., *Microbial Genetics Bull.*, **13**, 43 (1956).
¹⁹ Mardarowicz, C., *Z. Naturforsch.*, **216**, 1006 (1966).
²⁰ Work, E., *Biochem. J.*, **67**, 416 (1957).

Oxygen Isotope Profiles through the Antarctic and Greenland Ice Sheets

S. J. JOHNSEN, W. DANSGAARD & H. B. CLAUSEN

Geophysical Isotope Laboratory, Geophysical Institute, University of Copenhagen

C. C. LANGWAY, jun.

USA Cold Regions Research Engineering Laboratory, Hanover, New Hampshire

The Camp Century, Greenland, deep ice core reveals seasonal variations in the isotopic composition of the ice back to 8,300 years BP. This is not the case for the Byrd Station, Antarctica, deep ice core. Both cores show long-term perturbations in isotopic composition reflecting climatic changes from before the beginning of the last glaciation. But the complexity of the glaciological regime at Byrd Station precludes a rational choice of a time scale. Pole-to-pole correlations of the palaeoclimatic data therefore become speculative except for the more pronounced features and general trends.

DEEP ice cores contain palaeoclimatic information in the form of stable isotope variations¹⁻⁴. The isotopic composition of polar glacier ice (the ¹⁸O/¹⁶O ratio of melted ice samples measured mass spectrometrically) given in the δ scale⁵ depends chiefly on the temperature of formation of the snow at the time of deposition on the surface of an ice sheet. Increasing values upwards in a vertical ice core reflect a warming trend of the climate during the period of deposition. But other parameters influence the isotopic composition of the ice to some degree¹ and therefore caution should be used in translating the temporal δ variations found along an ice core into temporal temperature variations, although the present correlation between δ and temperature^{6,7} might be applicable over relatively short periods of time.

So far only two deep ice cores have been recovered completely through ice sheets: one at Camp Century, North-West Greenland⁸, the other at Byrd Station, West Antarctica⁹. Both

cores have been objects of preliminary isotope studies^{1,2}. The principal conclusions are that both cores reach back to before the last glaciation (Wisconsin, Würm).

Most if not all of the major climatic changes occurring within the past 100,000 yr (known from other geochronological studies) were recognized as variations in the Camp Century core. This core, treated in detail elsewhere^{3,4}, suggests climatic oscillations with periods of 2,400, 400, 180 and 78 yr, all of which appear to be caused by varying solar activity. On this basis one would also expect that the same oscillations should show up in a δ profile from an ice core through the Antarctic ice sheet, if the core is recovered from a region comparable with North-West Greenland with respect to accumulation, topography and steady state conditions.

No radioactive method exists for dating polar ice core older than roughly 1,000 yr (the half lives of tritium and ²¹⁰Pb are too short to allow dating of ice older than 100 yr; ³²Si may be used back to 1,000 yr; but ¹⁴C dating requires a large amount of fracture free ice). In principle, one might instead use the seasonal variations of the stable isotope concentrations in the accumulating snow and ice, counting summer layers characterized by relatively high δ values. (Other methods for determining annual layers at great depths are described in ref. 10. These methods are all less reliable than the stable isotope method.) But some eight isotope analyses are required for the identification of each annual layer, and such measuring frequencies are not practical over continuous deep core profiles. On the other hand, seasonal variations based on reasonably spaced increments of a deep ice core might show the relationship $\lambda = f(y)$ between the thickness, λ , of a given annual layer and its present distance, y , above the bottom. Age in years (t) could then be calculated as

$$t = \tau \int_H^{H-y} dy/f(y) \quad (1)$$

τ being the spacing (1 year, for example) and H the total thickness of the ice sheet.

This possibility of ice core dating raises the question of how long and to what degree the seasonal isotope variations in the

precipitation are preserved as an isotopic stratification of the firn and the ice. The most favourable conditions are obviously to be found on high polar glaciers with simple ice flow patterns and with considerable amounts of both summer and winter snow. The Camp Century ice core was recovered from such a glacier.

Fig. 1 shows a record of $\delta^{18}\text{O}$ in monthly precipitation samples collected at the nearby coast station Thule¹¹. The amplitude of the seasonal variations is of the order of 10 per mille (‰). This also holds for the upper annual layer of snow at Camp Century (Fig. 2a), but the amplitude is rapidly reduced to about 2‰ as the snow sinks to greater depths (Fig. 2b to e). All frequencies higher than 1 yr⁻¹ in the δ record have practically disappeared after 20 yr (Fig. 2b—this observation disagrees with isotope records, ref. 12, on the ice core from Site 2, not very far from Camp Century). This is because during compression of the porous surface snow (density 0.3 g cm⁻³) into impermeable ice (density 0.82 g cm⁻³ at 80 m depth), vertical air movement in the upper strata, due in part to air pressure changes, promotes a mass exchange between neighbouring layers. Diffusion of water in gaseous form may also contribute to the mass exchange, particularly because considerable temperature gradients exist in the upper strata (see refs. 13, 14).

As soon as the air channels in the firn close off, further mass exchange takes place only by slow molecular diffusion in the solid ice. This is why the amplitude of about 1.5‰ remains essentially unchanged for thousands of years (Fig. 2c to e). Sometimes a very strong oscillation appears even at considerable depth (such as the last oscillations in Fig. 2e). At least two explanations are possible: first, the accumulation for this particular year was unusually high; second, during the summer after deposition a refrozen meltwater layer formed, which prevented or reduced vertical air movement and mass exchange between strata.

Fig. 2c shows part of the decennium with lowest average δ -value for the past 800 yr³. During a 3 year period, even the (smoothed) summer values were below -30‰. The period AD 1690–1700 is generally considered one of the coldest in historical time. Furthermore, Icelandic historical sources¹⁵ indicate that the winter AD 1694–95 was extremely cold. This is the basis for estimating the ages of the annual layers shown in Fig. 2c.

As the annual layers approach the rock bed (1,390 m below surface at Camp Century) they get thinner by plastic deformation¹⁵. The progressive thinning is noticeable from Figs. 2b to e, and becomes dramatic from 2e to g, corresponding to 776 m and 1,061 m depths, respectively. The thinning increases the isotope gradients in the ice, which makes the molecular diffusion more effective in obliterating the seasonal variations*. In Fig. 2f more of the isotope oscillations are just about to disappear. In the nearly 2,000 yr old ice shown in Fig. 2g several annual oscillations may be missing and the rest will soon be obliterated leaving only lower frequencies in the δ curve, such as the smoothed curve in Fig. 2g and the curves in Fig. 2h (shown expanded) and Fig. 2i (expanded).

Thus in principle dating of the Camp Century ice core by counting annual layers is possible to about the 1,060 m depth,

* The amplitude, A , of the seasonal oscillations can be calculated by following a series of regular annual layers that sink into the ice sheet. t , years after firnification the amplitude has changed from A_0 to

$$A = A_0 \exp \left(-4\pi^2 \int_0^t (D(t')/\lambda(t')^2) dt' \right)$$

$D(t')$ is the diffusion constant, which depends on the temperature of the annual layers at the time t' . Introducing the flow model, the temperature profile and the diffusion constants previously reported^{8,16,17}, this equation shows that at Camp Century a 10% reduction of A takes 5,000 yr, and a 50% reduction takes 8,000 yr. After 10,000 yr only 10% of A_0 is left. This is in fairly good agreement with the data in Fig. 2. On the other hand, it is difficult to determine the age of old ice from measurements of A because of the lack of knowledge about such parameters as initial accumulation and temperature history.

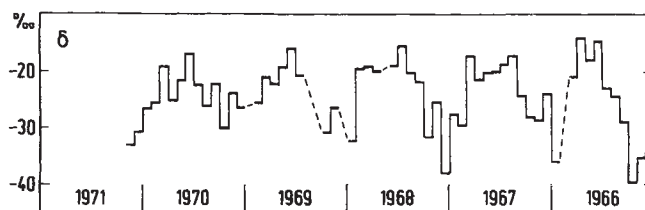


Fig. 1 The $^{18}\text{O}/^{16}\text{O}$ ratios (δ) of monthly samples of precipitation collected at Thule, North-West Greenland. The amplitude of the seasonal variation is of the order of 5 to 10‰.

corresponding to 8,300 yr BP according to the time scale which we shall adopt. It may be necessary, however, to apply a depth dependant correction to account for "lost" annual oscillations. Even during firnification seasonal δ -oscillations in years with unusually low accumulation may disappear due to mass exchange. Unfortunately, the physical condition (broken or missing pieces) of the Camp Century ice core precludes continuous measurement of seasonal isotope variations for the purpose of dating from the surface downward.

The physical condition of the Byrd Station ice core is considerably better. Nevertheless, as Fig. 3 shows, seasonal cycles

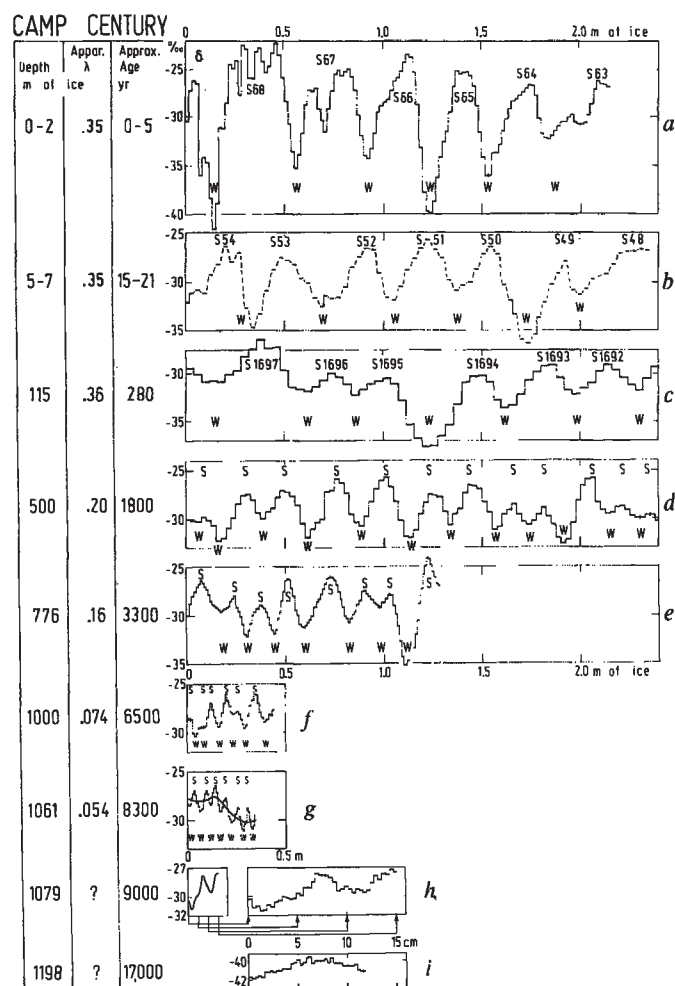


Fig. 2 The δ oscillations in firn and in ice cores from the depths below surface indicated to the left of the figure at Camp Century, 225 km east of Thule. S and W indicate interpretations of summer and winter layers, respectively. As the ice sinks towards the bottom, thickness, λ , of the annual layers is reduced due to plastic deformation. Within a few years (a and b) short-term δ variations are obliterated by mass exchange in the porous firn. After some decades (c and d) the seasonal δ amplitude is reduced to about 2‰. Further reduction takes place only by molecular diffusion in the solid ice and becomes effective only when, after thousands of years, the thinning of the layers has increased the δ gradients considerably (d to i).

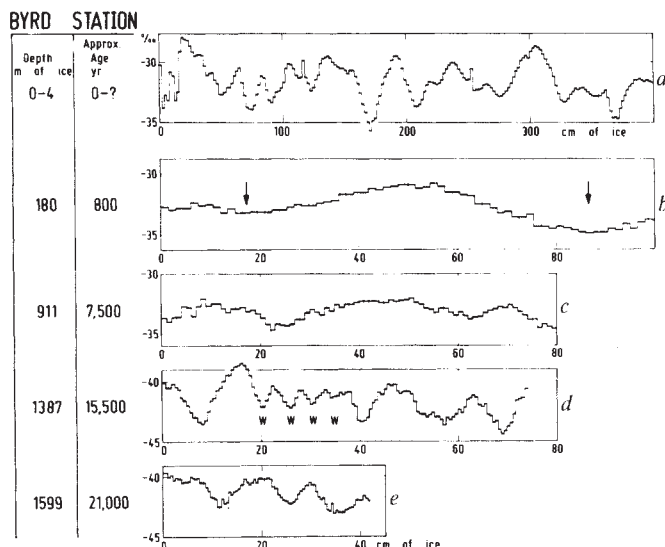


Fig. 3 The δ oscillations in firn and in ice cores from various depths below the surface at Byrd Station, Antarctica. Seasonal interpretation is difficult; *a* (note different depth scale) suggests mean accumulation rates between 40 and 18 cm of ice depending on the interpretation of summer peaks; *b-d* present similar difficulties, probably due to low and irregularly distributed accumulation in the source area.

are difficult to interpret in such low accumulation areas^{18,19}. The Byrd samples were cut to represent roughly 1.5 cm of accumulation (ice equivalent) in the upper strata (Fig. 3*a*) and diminishing with increasing depth as shown in Figs. 3*b* to *e*. Attempts to interpret successive summer and winter layers from these data lead to estimates of the accumulation ranging from 8 to more than 70 cm of ice per year. This is too irregular to justify dating of the Byrd core by means of the annual layers. It is interesting though that annual variations appear

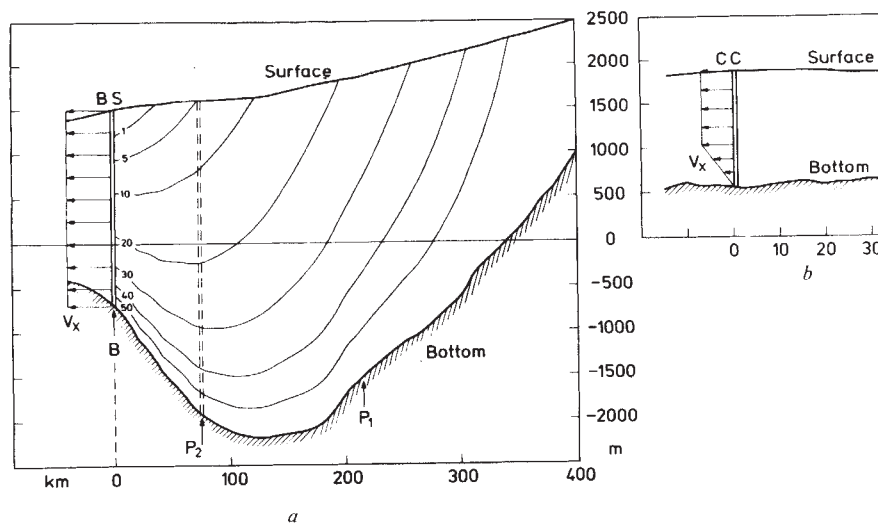
is nearly flat, and the thickness, H , of the ice sheet in the source area upstream is not very different from the value found at Camp Century ($H = 1,367$ m of ice equivalent). The horizontal velocity profile in a plane containing the bore hole approximates to that calculated²⁰ from the measured temperature profile⁸ and the mechanical properties of glacier ice²¹. The annual accumulation, λ_H , is fairly high (35 cm of ice equivalent²²) and varies only slightly in the source area²³. All of these factors are reflected in a simplified ice flow pattern in the Camp Century case and, therefore, permit a first approximation to the calculation¹⁶ of the age, t , of a core increment now situated y metre above the bottom:

$$t = \begin{cases} \frac{(2H-h)\tau}{\lambda_H} \ln \frac{2H-h}{2y-h}; & H > y > h \\ t_{y=h} + \frac{(2H-h)\tau}{\lambda_H} \left(\frac{h}{y} - 1 \right); & h > y > 0 \end{cases} \quad (2)$$

τ is 1 yr, and h ($=400$ m) is the distance from the bottom above which the horizontal velocity component is assumed to be uniform. The preliminary time scale given by (2) implies that λ_H , H and h have been constant in time. The δ variations along the Camp Century ice core are shown in Fig. 5*d*, plotted in a corrected time scale. The procedure for correcting the preliminary time scale along the Camp Century core has been described previously in detail⁴. It is based on Fourier spectral analysis completely independent of the preliminary scale and rests on two assumptions: namely, that the oscillations observed are caused by varying solar activity and that their periods have been constant in time.

In contrast to Camp Century, the glaciological regime at Byrd Station, Antarctica, is very complicated: H varies by a factor of almost 2 in the source area²⁴⁻²⁶ (Fig. 4*a*); λ_H varies not only upslope from the station (values between 12 and 28 cm have been reported²⁶), but also locally around the station (9 to 28 cm); melting from the bottom^{24,25} has removed many

Fig. 4 Approximate surface and bottom topographies in the Byrd Station (left²⁴) and the Camp Century (right²⁷) source areas. The thin curves are calculated flow lines. The assumed horizontal velocity profiles along the two ice cores (BS and CC) are shown by v_x . Bottom melting is assumed to take place from P_1 to P_2 , and refreezing from P_2 to B . The figures along the BS core indicate the approximate travel time of the ice in thousands of years. Flow model calculations are much more complicated for the Byrd Station than for the Camp Century location.



most distinctly in part of Fig. 3*d* representing a core increment approximately 15,000 yr old, much older than required for obliteration of annual layers in the Camp Century core. The probable reason is that the annual layers in the Byrd region only very slowly become thin enough to establish the gradients necessary to make the diffusion effective.

A preliminary time scale for the Camp Century core was established by model calculations of the ice flow pattern for the location. Fig. 4*b* shows schematically a vertical section of the North Greenland ice sheet in a direction close to that of the flow lines passing through Camp Century. The sub-ice surface

thousands of the annual accumulation layers; refreezing of meltwater occurs in part of the source area*; the distance,

* The only existing estimate^{24,25} suggests that 9 m of ice melted from the bottom during movement from P_1 to P_2 (Fig. 4*a*). The usual steady-state boundary conditions dictate that the thickness of an annual layer at the sub-ice interface approaches zero. Bottom melting destroys this boundary condition at B , and the 5 m of silty ice found near the bottom is probably a mixture of refrozen meltwater/soil. As the vertical strain between P_2 and B reduces the core length by a factor of 2, the 9 m of annual layers lost by the previous melting between P_1 and P_2 is approximately substituted by the 5 m of silty ice. This coincidentally re-establishes the boundary condition at B to its original state.

x , to the ice divide (a value which is essential for the ice core time scale due to the varying H) is poorly defined and may even be time dependent; and the horizontal spreading (divergence), of the ice flow is unknown and probably varies both with depth and along a flow line*.

Therefore, any mathematically determined time scale for the length of the Byrd core, based on available flow and accumulation data, contains large uncertainties. This holds particularly true when applying the simplest flow model of all²⁸. The consequent time scale²⁹:

$$t = \frac{H\tau}{\lambda_H} \ln \frac{H}{y} \quad (3)$$

implies no melting, and temporal as well as spacial constancy of both H and λ_H over the entire source area. In our opinion, equation (3) is only applicable on a major part of the Byrd core as a basis for a rough approximation such as we require for a systematic cutting of increments for isotope analysis. Three thousand samples were cut from the Byrd core in a continuous sequence, with varying lengths for different age intervals, according to equation (3) with $H=2,164$ m and $\lambda_H=13$ cm (Table 1).

Table 1 Sample Cutting Scheme for the Byrd Station Ice Core

Distance from the bottom y (m)	Cutting lengths (equivalent years according to equation (3))	Age intervals (yr according to equation (3))
2,110 to 1,757	12.5	500 to 3,500
1,757 to 848	25	3,500 to 16,000
848 to 409	50	16,000 to 27,800
409 to 4.8	100	27,800 to 102,000

The complete δ profile of the Byrd core plotted according to equation (3) is shown in Fig. 5a. In agreement with other studies the termination of the Wisconsin glaciation appears at about 10,000 yr BP. We feel that this agreement is fortuitous, and this becomes clear when the varying H is taken into account. Numerical integrations give the flow lines and the travel times of ice particles from their sites of deposition to the Byrd location. The δ profile plotted in the resulting time scale (that is, with $H=H(x)$) is shown in Fig. 5b. The termination of the Wisconsin glaciation in this case is almost 20,000 yr BP, which is far from an acceptable age.

Attempts to use spectral analyses for correcting the time scale on the Byrd core were not successful over the entire core length. The 2,400 yr period found in the Camp Century core did not show up in the Byrd record when plotted on the preliminary time scale, probably due to some of the complications mentioned earlier (when the Byrd record was plotted in the time scale proposed below, the 2,400 yr period did show up in the time interval covering the past 20,000 yr).

To establish a reasonable time scale for the Byrd core, we looked instead for some comparable δ variations in the two cores that would seem to originate from the same periods of time. In the Camp Century curve (Fig. 5c) the last interstadial in full glacial times ended at 13,000 BP, only a few hundred years before the main increasing tendency of the δ

curve began. Superimposed on this is a peak, indicated as the Allerød sequence, that ended 11,000 BP^{30,31}. The Byrd curve in Fig. 5a shows similar events at 14,800 and 12,200 BP respectively. In addition, the Byrd curve plotted between 83,000 to 69,000 BP is characterized by a long interstadial succeeded by a short one. We are inclined to correlate these two interstadials with the Brørup-Odderade sequence³², shown in Fig. 5e, and to use the short cold period between them (73,000 BP in Fig. 5a; 65,700 BP in Fig. 5e) as another fixed point (in addition to those at the end of Wisconsin mentioned above) in an attempt to correlate the Byrd time scale with the better founded Camp Century time scale.

The flow lines shown in Fig. 4a indicate the tracks of snow crystals from their sites of deposition to the Byrd location. They were calculated stepwise by making the following simple assumptions. Steady state conditions; surface and bottom topography as shown in Fig. 4a; ice divide situated 400 km upstream from Byrd station; uniform accumulation pattern and uniform divergence of flow in the entire source area; and uniform vertical strain rate at any given locality (this implies no melting or refreezing at bottom). A numerical integration of distance over velocity along the flow lines gives the total travel times and, thereby, the age-depth relationship along the Byrd core. Various values of λ_H and divergent (spreading) ice flow were used. A fit between the selected features of the Byrd and the Camp Century δ records at roughly 10,800, 13,500, and 65,600 BP was obtained for $\lambda_H=21.4$ cm of ice and a divergence of $d=2.5$. We emphasize that these values correlate only the selected features of the two ice core records (at the onset and the termination of the Wisconsin). Other values may be more appropriate to use on minor parts of the Byrd core. The resulting time scale applied to the δ record shown in Fig. 5c is not independent of the Camp Century time scale. Furthermore, it still implies dubious assumptions, such as λ_H being independent of t and x and that the melting and refreezing along the subsurface have always counterbalanced each other at B in Fig. 4a. Therefore, the Byrd time scale may incorporate considerable errors, in particular at the greater depths. This also holds for the time scale used in Fig. 5d ($\lambda_H=18.3$ cm, $d=1.55$, which places the end of another late glacial interstadial at 11,000 BP). Within the past 20,000 yr the curve in Fig. 5c contains cycles similar to the 2,400 yr cycles in the Camp Century curve. On the other hand, the time scale in Fig. 5d is based on a more likely value of the ice flow divergence. The assumed accumulation rates agree reasonably well in both cases with the 22 cm of ice per year required to make calculated temperatures fit with the observed temperature profile along the Byrd bore hole²⁵. Either of the two suggested time scales (Fig. 5c and d) is therefore a possible solution to the chronology problem of the Byrd core. A better overall approximation can hardly be obtained until the technique for carbon-14 dating of ice *in situ* becomes perfected³³, or more data on the complex accumulation and ice flow patterns become available.

Because of the procedures followed, it is not realistic to use the Byrd record for establishing the exact time interval represented by the Wisconsin glacier stage in Antarctica nor intervening events. What does appear clearly, however, is that in terms of δ variations, Camp Century was more sensitive than Byrd Station to glacial, as opposed to interglacial, conditions. The shift in δ level during the transition period was from -42 to -29‰ at Camp Century, compared with -41 to -34‰ at Byrd. This might be explained by the climatic conditions in North-West Greenland being heavily influenced by the extinction of the North American ice sheet, which 18,000 years ago covered a larger area than the Antarctic ice sheet does today³⁴.

In Fig. 6 the two δ records are compared in detail for the last estimated 20,000 yr in the time scales of Fig. 5c and e. The short term δ oscillations during late glacial time are more pronounced in the Camp Century record than in the Byrd record, whereas the δ curve for the post-glacial period at Byrd shows a more pronounced variability than does the Camp

* The ice, which formed far upstream from Byrd Station, has to pass the deep valley (Fig. 4a) before it reaches the drilling site. During the first (last) part of this passage, the vertical strain is much lower (higher) than in the case of a uniform thickness H . This means that the velocity, $v(x)$, of the ice passing through the valley, strongly influences the time scale of the Byrd core. At a given distance, x , from the ice divide $v(x)$ may be approximated by $\lambda_H \cdot x/H(x) \cdot d$, where d = divergence. Parallel flow ($d=1$) thus corresponds to velocities twice those of radial flow ($d=2$). Values of d between 0 and 1 correspond to convergent flow.

Century curve. A possible explanation for the stable character of the Camp Century curve in the post-glacial is the stabilizing effect of the open Baffin Bay close to Camp Century. Another interesting difference between the two records shown in Fig. 6 is that the post-glacial climatic optimum is revealed at Camp Century, whereas the post-glacial Byrd Station record shows pronounced oscillations and a shift in δ from -34‰ up to -33‰ after about 2,500 BP. The reason for this is not clear, particularly since the post-glacial climatic optimum

between 8,000 and 4,500 BP has been recognized in the southern hemisphere^{3,5}. The generally increasing tendency of the δ -curve was also noticed by Epstein *et al.*² who suggested it was due to the deeper strata originating from higher altitudes (with lower temperatures of deposition). But from Fig. 4a, assuming steady state, we see that the 5,000 yr old strata in the Byrd core was formed at an altitude of less than 50 m higher than the 2,000 yr strata, corresponding to a temperature difference of less than 0.5°C , that is, not enough to explain a

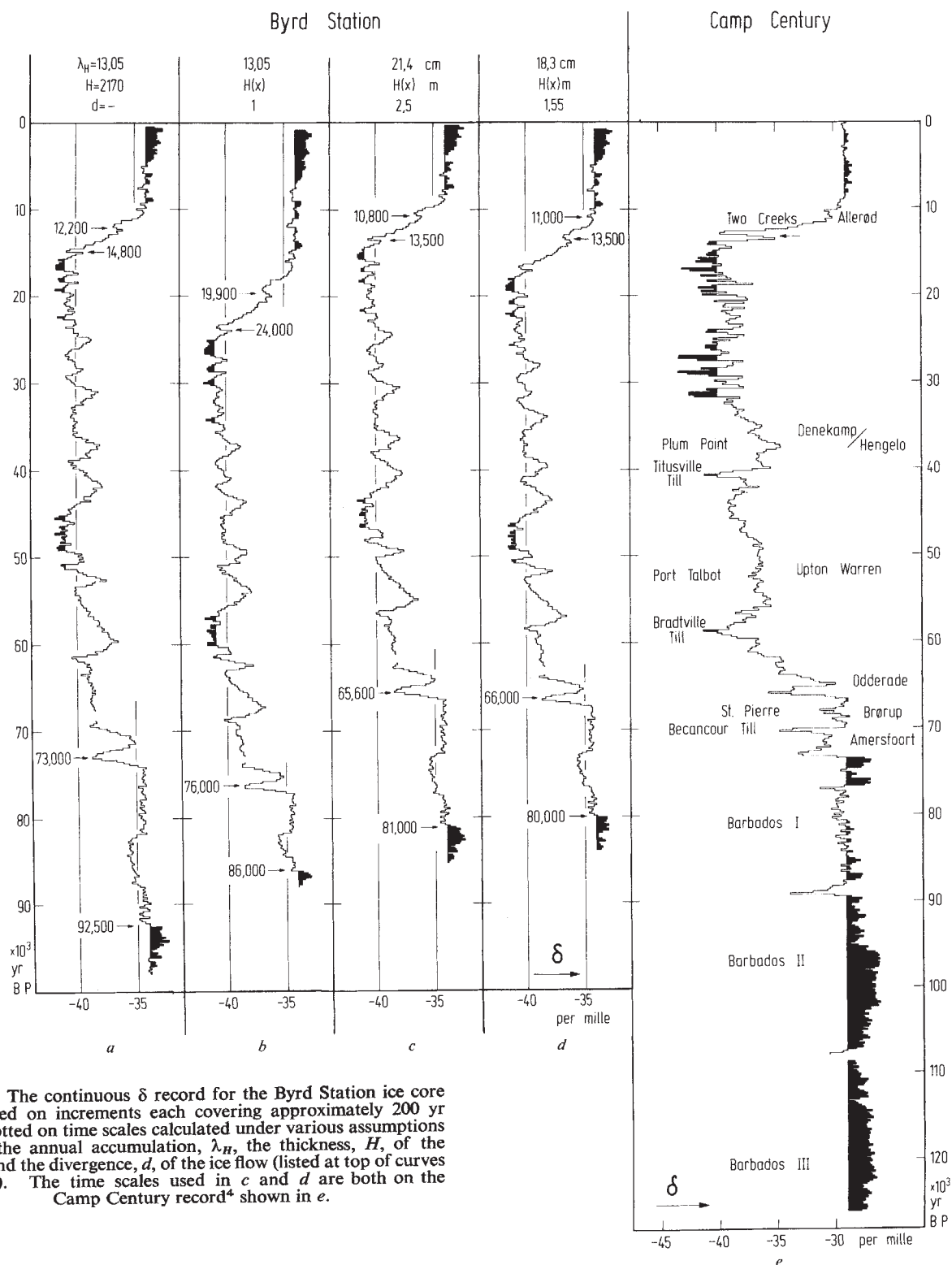


Fig. 5 The continuous δ record for the Byrd Station ice core measured on increments each covering approximately 200 yr and plotted on time scales calculated under various assumptions about the annual accumulation, λ_H , the thickness, H , of the sheet and the divergence, d , of the ice flow (listed at top of curves *a* to *d*). The time scales used in *c* and *d* are both on the Camp Century record⁴ shown in *e*.

difference of more than 1‰ in the δ s. Thus the assumption of steady state may not be valid. It seems more likely that the thickness of the ice sheet has diminished by a few hundred metres since the glaciation.

Apparently, because of the complicated glaciological regime existing at Byrd Station, interpretation of the Byrd core δ -record is not straightforward and contains many pitfalls. Because of the uncertainties involved, we feel that it is not advisable to attempt to compare the detailed interpretation shown for Camp Century in Fig. 5e with the Byrd record, nor to estimate possible phase differences between climatic fluctuations within the Wisconsin revealed by the two δ -records. Nevertheless, certain trends in the δ -records suggest a correlation with pronounced northern hemispheric climatic events, which has been used tentatively to adjust the time scale along the Byrd core.

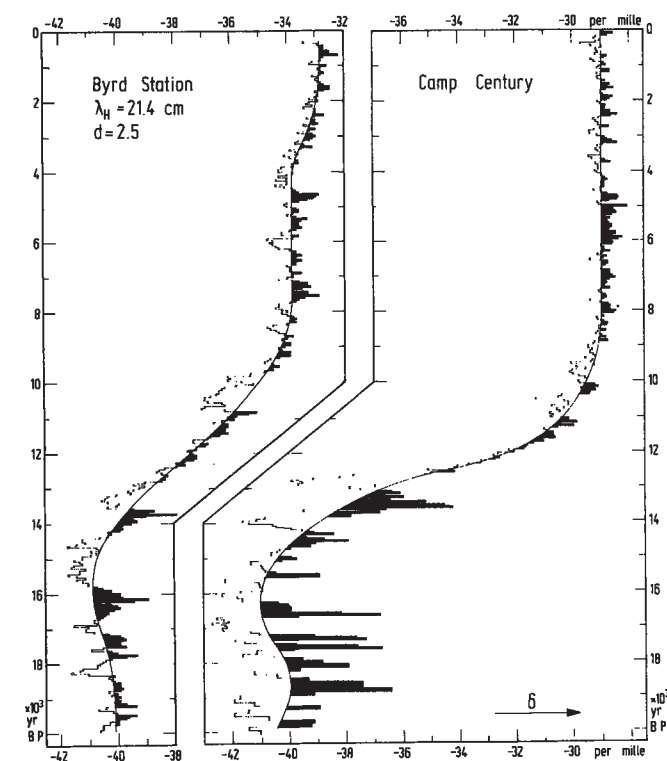


Fig. 6 The Byrd Station and Camp Century δ records measured in 50 yr sequences during the past 20,000 yr (according to the time scales used in Fig. 5c and e). The δ values exceeding the smoothed curves are set off in black. Relative to the Camp Century record, the Byrd Station shows less variation in the Wisconsin glaciation and a smaller shift in the transition period. Also note the difference in the post-glacial period.

Once again, we emphasize that caution should be used in translating the observed δ s into a temperature scale³⁶ because the deeper strata originated further inland, where slightly different climatic conditions existed; and because changes have occurred in the isotopic composition of seawater (which provides the moisture for the precipitation), the main meteorological pattern, the thickness of the ice sheet, the ice flow pattern and the ratio of winter to summer precipitation.

The present work contains two examples of deviation from the simple δ versus temperature relationship⁶: first, the δ difference between summer and winter deposits is rapidly reduced by mass exchange in the firn (Fig. 2), invalidating the initial representation of the difference between summer and winter temperatures; second, the increase in δ at Byrd from 4,000 to 2,500 BP (Fig. 6) does not reflect a warming trend³⁵, but rather a decreasing surface altitude of an ice sheet with a great negative mass budget. Furthermore, it should be noted

that the close δ versus temperature relationship observed in present day precipitation in Greenland is not generally valid in Antarctica^{6,37}, due to the complicated accumulation pattern and meteorological regime. Finally, the extinction of the Laurentide ice sheet completely changed the atmospheric circulation pattern at high northern latitudes. The climate of North-West Greenland changed from extremely continental into a more maritime character, whereby the present simple δ to temperature correlation was established. It is not justified to extend its validity to the glacial period.

In conclusion, the present geographical δ to temperature correlation should not be used quantitatively on temporal δ variations. But the excellent qualitative correlation of the entire Camp Century δ record with climatic events known from other independent sources shows clearly that isotope studies of deep ice cores is, nevertheless, a powerful paleo-climatological tool.

Financial support was provided by the Carlsberg Foundation, Copenhagen, and the US National Science Foundation, Office of Polar Programs.

Received November 24, 1971.

- ¹ Dansgaard, W., Johnsen, S. J., Møller, J., and Langway, C. C., *Science*, **166**, 377 (1969).
- ² Epstein, S., Sharp, R. P., and Gow, A. J., *Science*, **168**, 1570 (1970).
- ³ Johnsen, S. J., Dansgaard, W., Clausen, H. B., and Langway, C. C., *Nature*, **277**, 482 (1970).
- ⁴ Dansgaard, W., Johnsen, S. J., Clausen, H. B., and Langway, C. C., in *Late Cenozoic Ice Ages* (edit. by Turekian, K. K.), 37 (Yale University Press, 1971).
- ⁵ Craig, H., *Science*, **133**, 1833 (1961).
- ⁶ Dansgaard, W., *Tellus*, **16**, 436 (1964).
- ⁷ Picciotto, E., de Maere, X., and Friedman, T., *Nature*, **187**, 857 (1960).
- ⁸ Hansen, B. L., and Langway, jun., C. C., *Antarctic J. US*, **1**, 207 (1966).
- ⁹ Ueda, H., and Garfield, D., *US Army Cold Regions Research and Engineering Laboratory Tech. Rep. 231*, 1 (1969).
- ¹⁰ Langway, C. C., *The Geological Society of America, Special Paper*, **125**, 186 (1970).
- ¹¹ Environmental Isotope Data, *Tech. Rep. Ser. No. 117* (IAEA, Vienna, 1970).
- ¹² Epstein, S., and Sharp, R. P., *Amer. Geophys. Union Trans.*, **40**, 81 (1959).
- ¹³ Yen, Y. C., *J. Geophys. Res.*, **4**, 1093 (1963).
- ¹⁴ Benson, C., *USA Snow, Ice and Permafrost Res. Establ., Res. Rep. 70*, 93 (1962).
- ¹⁵ Einarsson, M. A., and Hafisinn, *Alm. Bokaf.* (Reykjavik, 1969).
- ¹⁶ Dansgaard, W., and Johnsen, S. J., *J. Glaciol.*, **8**, 215 (1969).
- ¹⁷ Ramseier, R. O., *USA Cold Regions Research and Engineering Laboratory Res. Rep. 232* (1967).
- ¹⁸ Gonfiantini, R., Togliatti, V., Tongiorgi, E., de Breuck, W., and Picciotto, E., *J. Geophys. Res.*, **68**, 3791 (1959).
- ¹⁹ Epstein, S., and Sharp, R. P., *Intern. Assoc. Sci. Hydrol. Pub.*, No. 58, 273 (1962).
- ²⁰ Weertman, J., *J. Geophys. Res.*, **73**, 2691 (1968).
- ²¹ Jones, S. J., and Glen, J. W., *J. Glaciol.*, **8**, 463 (1969).
- ²² Crozaz, G., and Langway, jun., C. C., *Earth Planet. Sci. Lett.*, **1**, 194 (1966).
- ²³ Mock, S. J., *J. Glaciol.*, **7**, 59 (1968).
- ²⁴ Budd, W. F., Jensen, D., and Radok, U., *Polarforschung*, **6**, 293 (1969).
- ²⁵ Budd, W. F., Jensen, D., and Radok, U., *Univ. Melbourne Pub.*, **18**, 178 (1971).
- ²⁶ Bentley, C. R., Cameron, R. L., Bull, C., Kojime, K., and Gow, A. J., *Amer. Geog. Soc. Antarctic Map Folio Series, Folio 2*, Plate 4 (1964).
- ²⁷ Robin, G. de Q., Evans, S., and Bailey, J. T., *Phil. Trans. Roy. Soc. A*, **265**, 437 (1969).
- ²⁸ Nye, J. F., *J. Glaciol.*, **3**, 493 (1959); **4**, 785 (1963).
- ²⁹ Haefeli, R., *J. Glaciol.*, **3**, 1133 (1961).
- ³⁰ Iversen, J., *Geol. Survey of Denmark, Ser. II*, 80 (1954).
- ³¹ Tauber, H., in *Nobel Symp. 12, Radiocarbon Variations and Absolute Chronology* (edit. by Olsson, I. U.) (Wiley, New York, 1970).
- ³² Andersen, S. Th., *Geol. Survey of Denmark, Ser. II*, 75 (1960).
- ³³ Oeschger, H., Alder, B., and Langway, jun., C. C., *J. Glaciol.*, **6**, 939 (1967).
- ³⁴ Flint, R. F., *Glacial and Quaternary Geology*, 78 (Wiley, 1971).
- ³⁵ Auer, V., *Proc. Roy. Soc. B*, **152**, 507 (1960).
- ³⁶ Wilson, A. T., and Hendy, C. H., *Nature* (in the press).
- ³⁷ Lorius, C., *Com. Nat. Francais Rech. Antarct.*, **8**, 1 (1963).

LETTERS TO NATURE

PHYSICAL SCIENCES

Rifting in Eastern Africa and the Fragmentation of Gondwanaland

THERE is a long history of rifting in eastern Africa and a complete system of faults has developed. Times of movement on rift faults, dated by palaeontological and geomorphological methods, cover a span extending back to the start of the Mesozoic. They show that periods of movement on some faults were separated by long periods of inactivity^{1,2}. This has given rise to the impression that a single rift system in eastern Africa has been activated intermittently since at least the start of the Mesozoic, and a hypothesis^{3,4} that all movements of this system are related to some permanent mantle feature under it.

During the Mesozoic rifting was most extensive in East-Central Africa and southern Tanzania, and there are few signs that areas north of Tanzania, apart from coastal Kenya, were affected. Since the Mesozoic, rifting has occurred throughout much of eastern Africa north of the Zambesi Valley, and is most extensive north of central Tanzania. These facts have given rise to a general impression that rifting was initiated in East-Central Africa and that the centre of activity has moved northwards with time. They have also led some people to wonder, why, since rifting has been taking place for a longer time in East-Central Africa, the rifts in that area do not appear more developed structurally than some rifts in East Africa.

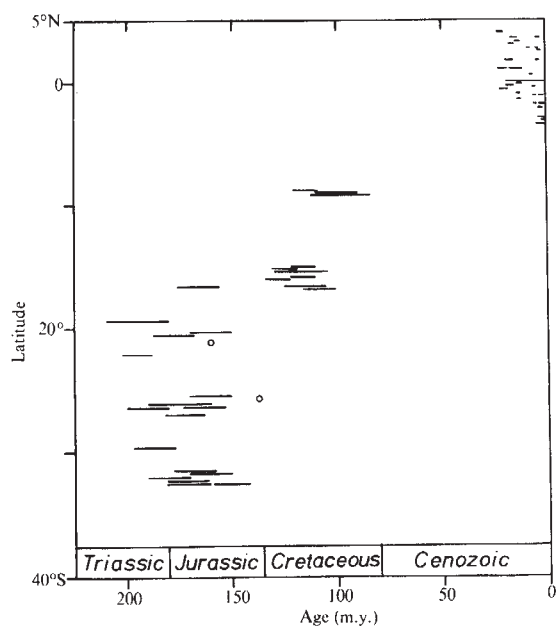


Fig. 1 K-Ar and Rb-Sr radiometric ages for igneous rocks from East and East-Central Africa plotted against geographic latitude. Horizontal bars represent ages with error in determination. Ages published without error in determination are shown as open circles. Sources: refs. 5-7 (review), 8 and 9.

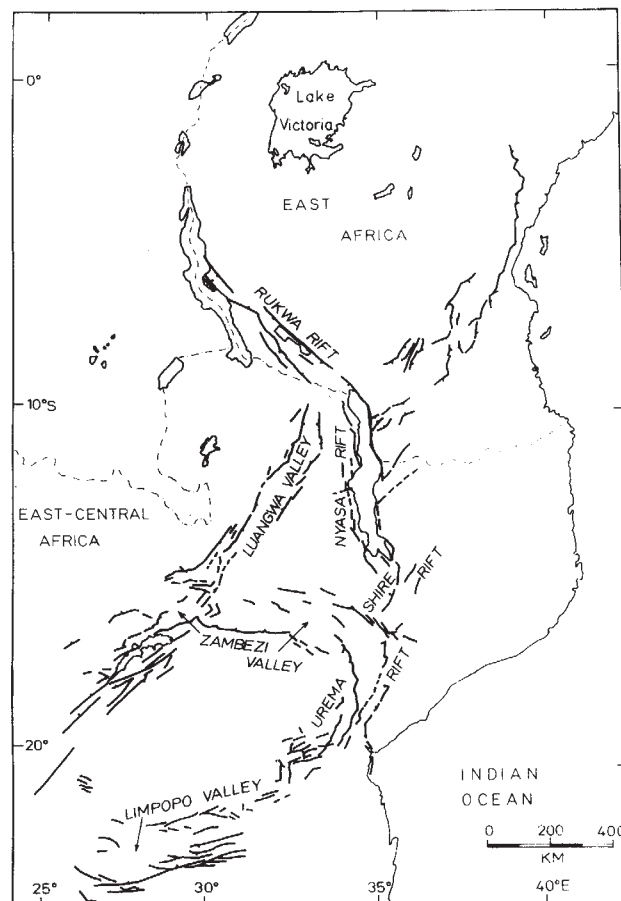
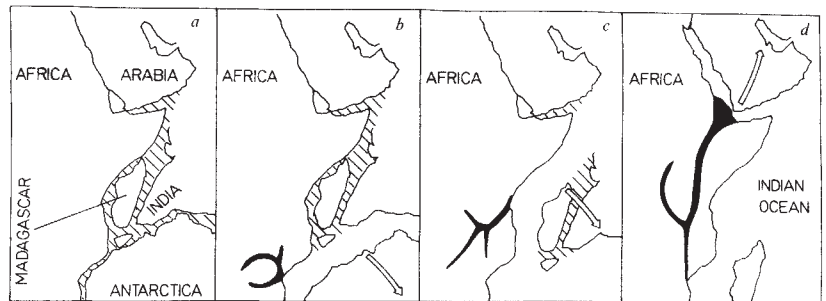


Fig. 2 Rift faults in East and East-Central Africa which are active in the Mesozoic. Sources: refs. 1, 2, 5 and 18.

Alkaline and per-alkaline igneous activity occurred in eastern Africa during times of rift faulting in both the Mesozoic and Cainozoic and some products of this activity have been dated radiometrically. The number of ages determined is sufficient to allow a rough estimate of the times and duration of the major periods of rifting to be made. When published ages⁵⁻⁹ are plotted against geographic latitude (Fig. 1), they fall into three groups. The oldest, intermediate and youngest age groups are given by specimens from areas respectively south, at either end, and north of Lake Nyasa. This grouping suggests that since the start of the Mesozoic a distinct period of rifting occurred in the Triassic-Jurassic, another in the Cretaceous, and one since the mid-Cainozoic. The plot provides little evidence that the sites of rift activity have moved systematically during individual periods of rifting, but shows that the centre of activity during successive periods has been located progressively further north. Igneous rocks indicative of rifting, and dated stratigraphically as Cretaceous, occur in coastal East Africa between latitudes 4° to 8° S (refs. 10 to 13). Radiometric ages for these are not available and so could not be plotted.

Fig. 3 Suggested connexions between rifting in eastern Africa and the breakup of Gondwanaland. Black shaded areas represent main fault zones in Africa active during different stages of breakup. *a*, Relevant parts of a reconstruction of Gondwanaland for end-Palaeozoic time (after Smith and Hallam²²). *b*, Breakup of Antarctica and Africa (Triassic-Jurassic). *c*, Breakup of Madagascar and Africa (Cretaceous). *d*, Breakup of Arabia and Africa (mid-Cainozoic to present).



There is little doubt that the rifting between mid-Cainozoic and the present day in eastern Africa is associated with continental breakup and seafloor spreading along the Red Sea and Gulf of Aden¹⁴. Because this breakup only began in approximately the mid-Cainozoic¹⁵⁻¹⁷, earlier periods of rifting in eastern Africa were either isolated tectonic events or were related to continental breakup elsewhere. An attempt to distinguish between these alternatives may be made by seeing if faults active during the Mesozoic are in regions where continental breakup was occurring at the appropriate times.

A map of major rift faults active during the Mesozoic (Fig. 2) shows faults near the eastern coast of Africa in southern Mozambique and in East Africa. It has been suggested¹⁹ that rifts in the vicinity of southern Mozambique may be associated with continental breakup in nearby offshore regions. The proximity of Mesozoic faults to the East African coast could possibly be similarly explained as associated with breakup offshore from East Africa.

The geological development of the western Indian Ocean has recently been discussed in articles about Gondwanaland²⁰⁻²³. In reconstructions of Gondwanaland for end-Palaeozoic time continents are arranged along the eastern side of Africa in one of two main ways. In one²³, Madagascar occupies its present position relative to Africa and a wide strip of Indian Ocean borders eastern Africa. In the other²⁰⁻²², Madagascar occupies the embayment in the coastline of East Africa, part of Antarctica the embayment near southern Mozambique, and the Indian Ocean does not exist (Fig. 3*a*). Clearly any attempt to relate Mesozoic rifting in Africa with breakup of Gondwanaland will depend on which of these reconstructions is considered.

With the first reconstruction it is difficult to envisage a direct relationship because breakup or seafloor spreading in the Mesozoic would have occurred roughly 1,600 km east of the nearest known Mesozoic rift faults. To support this reconstruction it has been inferred²³ from the presence of late-Palaeozoic sediments in neighbouring parts of Africa and Madagascar² that the entire intervening region existed at the end-Palaeozoic. This inference is questionable. Comparable Mesozoic sediments occur along the shores of the Red Sea¹⁵⁻¹⁷, yet part of the crust beneath the Red Sea has formed only since the mid-Cainozoic. The coasts of East Africa and western Madagascar could have been a zone of structural weakness and a trough of sedimentation for a considerable time prior to breakup, as the site of the Red Sea appears to have been.

With the second reconstruction, which is supported by recent geophysical results²⁴, the lines of breakup would have been only roughly 150 km from the present coast of East Africa. Smith and Hallam²² give geological evidence for this reconstruction. They also show, partly from the presence of igneous rocks along coastal eastern Africa, that Antarctica broke away from Africa in the Upper Triassic-Lower Cretaceous interval whereas Madagascar did not break away until the Upper Cretaceous.

I conclude that sufficient data now exist to show that the extensive series of rift faults, known collectively as the East African rift system, results from three separate periods of rifting, and that these periods were associated with the frag-

mentation of Gondwanaland. The first period occurred in the Triassic-Jurassic associated with the breakup of Antarctica and Africa, the second in the Cretaceous associated with the breakup of Madagascar and Africa, and the third began in the mid-Cainozoic associated with the breakup of Arabia and Africa. The latter is still in progress. The main areas of Africa where rift faulting probably occurred during the different periods are shown in Fig. 3.

These conclusions are consistent with the centre of rift activity in eastern Africa having moved northwards with time, but not with the view that the periods of rifting are related by some permanent feature of the mantle localized beneath eastern Africa. If the periods of rifting are related at all, it is because each is associated with a stage in the fragmentation and dispersal of Gondwanaland.

The degree of structural development of continental rifts is apparently related to the amount of lateral extension which has occurred across them. Accepting the earlier conclusions, the probable places in eastern Africa where maximum extension occurred during each period are widely separated. Furthermore, as successive extension directions will have been approximately N-S, NW-SE, and E-W, differing by between roughly 45° and 90°, rifts which experienced large components of extension during one period will have experienced smaller components during the other two. I suggest that while rifting in East-Central Africa has occurred for a longer total time than in East Africa, less extension has occurred across individual rifts, and this is the main reason they are structurally less developed than some rifts in East Africa.

I thank Dr A. C. McLean for critical reading of the manuscript.

W. T. C. SOWERBUTTS

Department of Geology,
The University of Glasgow,
Glasgow W2

Received November 10; revised December 9, 1971.

¹ Dixey, F., *Quart. J. Geol. Soc. Lond.*, **102**, 339 (1946).

² Dixey, F., *Col. Geol. Min. Res. Bull.*, Suppl. 1 (1956).

³ McConnell, R. B., *Nature*, **215**, 578 (1967).

⁴ McConnell, R. B., *Graben Problems* (edit. by Illies, J. H., and Mueller, St.), 285 (Schweizerbart, Stuttgart, 1970).

⁵ Vail, J. R., *Geol. Rdsch.*, **57**, 601 (1967).

⁶ Woolley, A. R., and Garson, M. S., *African Magmatism and Tectonics*, (edit. by Clifford, T. N., and Gass, I. G.), 237 (Oliver and Boyd, Edinburgh, 1970).

⁷ Baker, B. H., Williams, L. A. J., Miller, J. A., and Fitch, F. J., *Tectonophysics*, **11**, 191 (1971).

⁸ Evans, A. L., Fairhead, J. D., and Mitchell, J. G., *Nature Physical Science*, **229**, 19 (1971).

⁹ Gromme, C. S., Reilly, T. A., Mussett, A. E., and Hay, R. L., *Geophys. J.*, **22**, 101 (1971).

¹⁰ Spence, J., *Geol. Surv. Tanzania, Bull. No. 28* (1957).

¹¹ Halligan, R., *Rec. Geol. Surv. Tanganyika*, **6**, 17 (1958).

¹² Kent, P. E., and Hunt, J. A., *The Geology of Coastal Tanzania* (in the press).

¹³ Caswell, P. V., and Baker, B. H., *Rep. Geol. Surv. Kenya, No. 24* (1953).

¹⁴ McKenzie, D. P., Davies, D., and Molnar, P., *Nature*, **226**, 243 (1970).

¹⁵ Whiteman, A. J., *Geol. Mag.*, **105**, 231 (1968).

¹⁶ Dubertret, L., *Phil. Trans. Roy. Soc., A*, **267**, 9 (1970).

¹⁷ Swartz, D. H., and Arden, D. D., *Bull. Amer. Assoc. Petrol. Geol.*, **44**, 1621 (1960).

- ¹⁸ Kennerley, J. B., *Fault Map of Tanzania* (Institute of Geological Sciences, London, 1967).
¹⁹ Cox, K. C., *African Magmatism and Tectonics* (edit. by Clifford, T. W., and Gass, I. G.), 211 (Oliver and Boyd, Edinburgh, 1970).
²⁰ Dietz, R. S., and Holden, J. C., *J. Geophys. Res.*, **75**, 4939 (1970).
²¹ McElhinny, N. W., *Nature*, **228**, 977 (1970).
²² Smith, A. G., and Hallam, A., *Nature*, **225**, 139 (1970).
²³ Tarling, D. M., *Nature*, **229**, 17 (1971).
²⁴ Hiertzler, J. R., and Burroughs, R., *Science*, **174**, 488 (1971).

Low Angle Electron Scattering from Carbonized Polymer Fibres

MANY observations have been made on carbon or "graphite" fibres by the technique of small angle X-ray scattering¹⁻³. Valuable as these observations are for the investigation of mean scattering parameters from a bundle of fibres they cannot normally be made on single fibres, nor can they easily be correlated with microstructural features in the fibre. For these reasons the technique of low angle electron scattering, carried out in an electron microscope, was expected to be more useful for single fibre studies.

Polyacrylonitrile co-polymer (PAN.C) fibres were oxidized for 5 h at 220° C and carbonized to a variety of heat treatment temperatures (HTT). Single fibres were then thinned by argon-ion bombardment and examined in a JEM 100B microscope at a camera length of 20 m. Two of the patterns obtained are

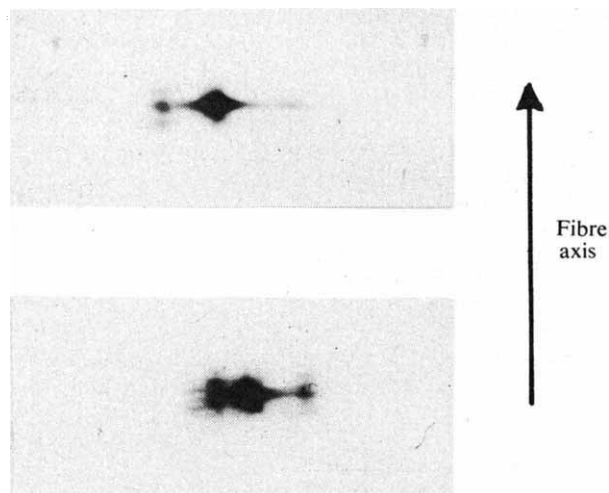


Fig. 1 Low angle electron scattering patterns from PAN.C fibres oxidized for 5 h at 220° C and then carbonized to 500° C.

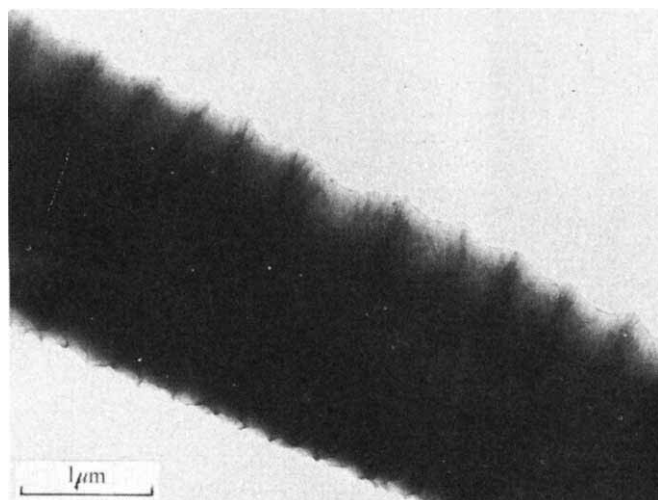


Fig. 2 A fibre carbonized to 400° C and ion-beam thinned.

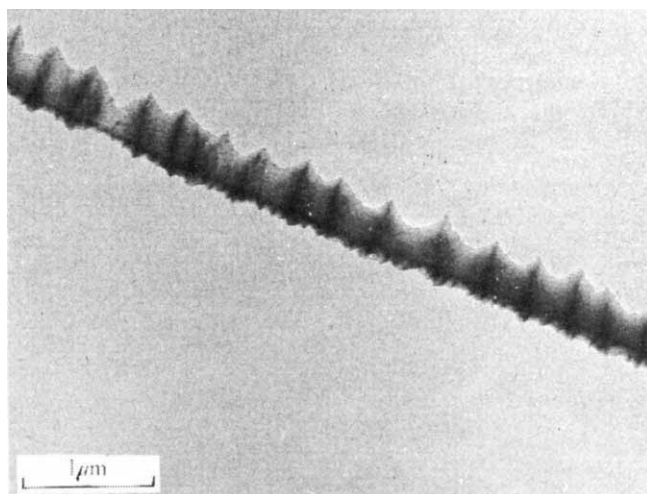


Fig. 3 A fibre carbonized to 500° C and ion-beam thinned.

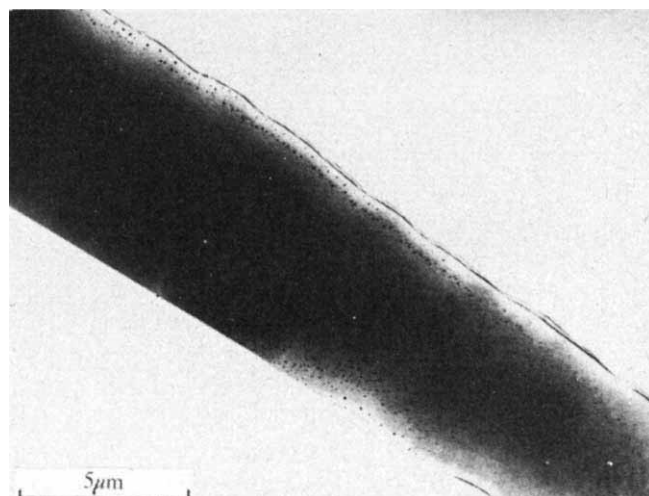


Fig. 4 "S" glass fibre after ion-beam thinning.

shown in Fig. 1. The characteristic features of the patterns are equatorial streaks, often exhibiting intensity maxima on both sides of the main beam, and off-equatorial intensity maxima, usually found either side of an equatorial maximum. These features were present in the patterns obtained from fibres at all stages of heat treatment. The maxima were not always symmetrically placed with respect to the main beam, however, nor indeed were they always present on both sides of the pattern.

Micrographs taken from part of the area contributing to the pattern are shown in Figs. 2 and 3. It can be seen that the thinned fibres are only ~1 μm wide and show a fairly regular structure along their axis, with a spacing in the range 250–600 nm. It is considered that the equatorial streak and intensity maxima in the scattering pattern arise from the shape transform of the fibre, since the illuminating beam of electrons has a diameter greater than the fibre width, but the off-equatorial scattering arises from the variation in structure along the axis of the fibre. The spacings of the off-equatorial maxima imply that the scattering features are 150–400 nm apart, which correlates well with the observed spacings in the micrographs.

Because ion bombardment is known to produce a surface structure even on originally flat surfaces⁴ I thought that the observed structure could have been formed during the thinning process. To check this a glass fibre of initially similar geometry was thinned by the same process, with the result shown in Fig. 4. Careful study of the micrographs from the two materials shows that there is a similar fine "ripple" structure on both

glass and carbonized polymer, but no evidence at all of the much larger scale structure in the glass fibre.

The origin of the structure in carbonized fibres is not clear. I have found no evidence that the spacing changes with HTT, although there is quite a wide scatter among fibres even at the same HTT. A variation in structure along the axis of stretched polymer has been reported previously both from PAN⁵ and oxidized PAN.^{6,7} but the period of these variations is an order of magnitude less than those reported here. Work is continuing in order to elucidate the structure of these features and also to investigate puzzling aspects of the low angle scattering patterns, such as the absence of zero order non-equatorial (meridional) scattering. Optical analogue experiments are in progress, aimed at separating effects attributable to the fibre shape transform from those due to structural features within the fibre.

I thank P. H. Warren for performing some of the early experiments which brought the problem to light and Professor J. E. Bailey for his interest.

P. J. GOODHEW

Department of Metallurgy and Materials Technology,
University of Surrey

Received October 6, 1971.

¹ Johnson, D. J., and Tyson, C. N., *Brit. J. Appl. Phys.*, **2**, 787 (1969).

² Johnson, D. J., and Tyson, C. N., *Brit. J. Appl. Phys.*, **3**, 526 (1970).

³ Perret, R., and Ruland, W., *J. Appl. Cryst.*, **2**, 209 (1969).

⁴ Trillat, J. J., *Ionic Bombardment: Theory and Applications* (Wiley, 1962).

⁵ Hinrichsen, G., and Orth, H., *J. Polymer Sci.*, **B**, **9**, 529 (1971).

⁶ Tyson, C. N., *Nature Physical Science*, **229**, 121 (1971).

⁷ Fillery, M. E., and Goodhew, P. J., *Nature Physical Science*, **231**, 118 (1971).

BIOLOGICAL SCIENCES

Structure of a Monomeric Oxygen-carrying Complex

THE geometry of the metal-oxygen linkage of myoglobin and haemoglobin has not been determined in detail. Recent studies of the reversible oxygen-carrying cobalt complexes, $\text{Co}(\text{acacen})(\text{B})\text{O}_2^{1,2}$ (acacen = $\text{N,N}'$ -ethylenebis(acetylacetoniminide), $(\text{CH}_3 - \text{C}(\text{O}^-) = \text{CH} - \text{C}(\text{CH}_3) = \text{NCH}_2 -)_2$, B = base; py and so on) and coboglobin³, the cobalt analogue of haemoglobin, indicate that the binding of oxygen in haemoglobin is essentially the same as that in the model 1 : 1 cobalt complexes. We now report the structure of a cobalt oxygen complex, analogous to $\text{Co}(\text{acacen})(\text{B})\text{O}_2$, that provides information on the metal-oxygen linkage, relevant to the structures of oxy-myoglobin and oxyhaemoglobin. This structure of $\text{Co}(\text{bzacen})(\text{pyridine})\text{O}_2$ (bzacen = $\text{N,N}'$ -ethylenebis(benzoylacetoneiminide), $(\text{C}_6\text{H}_5 - \text{C}(\text{O}^-) = \text{CH} - \text{C}(\text{CH}_3) = \text{NCH}_2 -)_2$, is shown in Fig. 1. As indicated by X-ray studies on oxymyoglobin⁴ and infrared and electron spin resonance (ESR) studies of $\text{Co}(\text{acacen})(\text{B})\text{O}_2$ (ref. 2), the oxygen molecule is bound to cobalt in an angular manner.

Crystals suitable for X-ray analysis were obtained by a method detailed elsewhere (J. D. Landels and G. A. R., unpublished work). One essential feature of this preparation was the need for solid starting material $\text{Co}(\text{bzacen})$ in the reaction mixture. All our preparations have yielded polycrystalline aggregates of thin, elongated triangular plates, usually with smaller plates growing out of their large surfaces so that their edge-on views resemble fir trees. The crystal ultimately selected for this study was 0.8 mm in maximum dimension and 0.06 mm thick. Its mosaicity, initially poor, deteriorated during the X-ray experiments which included three separate refinements of its orthorhombic unit cell constants. These altered in a statistically significant fashion,

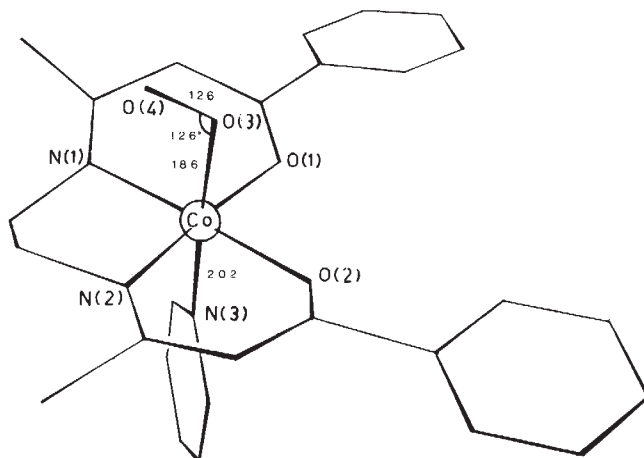


Fig. 1 Perspective view of the monomeric molecular oxygen complex $\text{Co}(\text{bzacen})(\text{pyridine})\text{O}_2$. (Bond lengths in pm, angle in degrees.)

probably directly attributable to the changing mosaicity, but possibly due to a more fundamental change within the crystal (such as an egress of molecular oxygen brought about by absorption of energy from the incident X-ray beam ($\lambda(\text{Mo K}\alpha)$ 71.07 pm). Accordingly these constants, and an associated range within which all of our determinations lie, are $a = 1,369 \pm 7$, $b = 821.5 \pm 0.9$, $c = 2,188 \pm 6$ pm. Systematic absences among all recorded spectra are consistent with either the centrosymmetric space group Pnma or the noncentric space group $\text{Pna}2_1$. This analysis substantiates that there are four molecules in the unit cell and that the non-centrosymmetric space group, $\text{Pna}2_1$, is probably correct.

Intensity data were collected on a Hilger and Watts 4-circle automatic diffractometer and figures given in this paper are based on 415 reflexions, in the sphere $0 < \theta \leq 18^\circ$, whose intensities exceeded three times their estimated standard deviations. The data were corrected for absorption and scaled according to values of standard reflexions used to monitor crystal decomposition. These standards had dropped to 87% of their starting values when reflexions in this shell had been collected.

Structure solution proceeded using normal heavy atom Patterson and difference Fourier techniques. Pyridine and phenyl rings were included, with their attached hydrogen atoms, as rigid groups in full-matrix least-squares refinements. Final R-factors were 6.3% with an ordered model in space group $\text{Pna}2_1$ and 7.4% with a disordered ethylene bridge in space group Pnma . This difference sustains the hypothesis that the non-centrosymmetric space group is correct at better than the 99.5% significance level⁵. Unfortunately there are too few data to refine all the parameters required to define the non-centrosymmetric model and still obtain accurate bond lengths and angles in the Schiff base ligand. The dimensions of the cobalt oxygen moiety, however, have remained constant (within their estimated standard deviations quoted in parentheses) throughout all refinement attempts in both space groups.

The structure consists of monomeric molecular units one of which is depicted in the figure. Coordination about cobalt is approximately octahedral with the four Schiff base ligand atoms coplanar with this metal atom. The normal to the pyridine ring and the $\text{O}(3) - \text{O}(4)$ vector are approximately coplanar and this plane bisects the $\text{N}(1) - \text{Co} - \text{N}(2)$ bond angle. This orientation of the oxygen molecule gives the maximum overlap of its π^* orbitals with $d\pi$ orbitals of cobalt, while the orientation of the pyridine ring would appear to minimize interaction with adjacent Schiff base atoms. The orthogonal relationship of the oxygen and pyridine planes may be important for the participation of π orbitals of pyridine in metal-ligand bonding. If this arrangement is a requirement for good oxygen binding it is possible that in myoglobin and haemoglobin, the O_2 molecule lies in a plane perpendicular to that of the

imidazole ring of the proximal histidine group. The imidazole plane approximately bisects the metal-nitrogen bond angles of the porphyrin group⁶. The orientation of the cobalt oxygen plane is also of significance in the interpretation of ESR results for the acacen complexes².

The dimensions of the metal-oxygen moiety have been the subject of a considerable amount of speculation. The 126(2)° bond angle observed for Co-O-O in this complex accords with that predicted by Pauling in 1948⁷ and differs from the alternative sideways coordination postulated by Griffith⁸ and observed for oxygen complexes of heavy metals⁹. The present O-O distance of 126(4) pm is comparable with the superoxide ion value (128 pm) and therefore in accord with the Co(III)-O₂⁻ formulation proposed from ESR studies². This distance is slightly shorter than that observed for bridged superoxo 1:2 oxygen cobalt complexes (131-135 pm)¹⁰⁻¹². The Co-O(3) and Co-N(3) bond lengths appear normal and the O(3)-Co-N(3) angle is 177(3)°.

Some inter or intramolecular interaction with the terminal oxygen atom O(4) might be expected in view of the strong tendency for oxygen to form 1:2 bridged complexes and its possible interaction with distal histidines in myoglobin and haemoglobin. However, in the present structure the closest non-hydrogen contacts with O(4) are intramolecular (N(1), N(2), ethylene carbon (290-300 pm)), and intermolecular with phenyl group carbon atoms (330 and 340 pm).

A significant feature of the structure is the approximate coplanarity of the phenyl substituents with the Schiff base-cobalt system. This could facilitate electron delocalization within the cobalt Schiff base group, thereby enabling greater π electron donation to the metal. This is considered to be an important factor in the stabilization of iron-oxygen coordination¹³. For this complex the overall spatial arrangement of the ligands, coupled with the evidence for net electron charge transfer from cobalt to oxygen², indicates the importance of π electron donation. It is possible that this plays a key role in producing the conformational changes about the iron atom that trigger rearrangement of the haemoglobin molecule on oxygenation¹⁴.

It may also be of value to note that the orientation of the pyridine ring in this complex is strikingly similar to that of the benzimidazole ring in vitamin B12 and its coenzyme^{15,16}. The structures of NN'-ethylenebis(salicylideneiminato)pyridine cobalt(II)¹⁷, di(cyclohexane-1,2-dioximato(1-))di-imidazole-iron(II)¹⁸, and O-methyl(Co-C)carboxymethyl(bisdimethylglyoximato)pyridinecobalt¹⁹ relate to that presented here.

G. A. RODLEY
WARD T. ROBINSON

Department of Chemistry,
University of Canterbury,
Christchurch, New Zealand

Received November 9, 1971; revised January 3, 1972.

- ¹ Crumbliss, A. L., and Basolo, F., *J. Amer. Chem. Soc.*, **92**, 55 (1970).
- ² Hoffman, B. M., Diemente, D. L., and Basolo, F., *J. Amer. Chem. Soc.*, **92**, 61 (1970).
- ³ Hoffman, B. M., and Petering, D. H., *Proc. US Nat. Acad. Sci.*, **67**, 637 (1970).
- ⁴ Watson, H. C., and Nobbs, C. L., *Nineteenth Coll. Ges. Biol. Chemie, Mosbach* (Springer, Berlin, 1968).
- ⁵ Hamilton, W. C., *Acta Cryst.*, **18**, 502 (1965).
- ⁶ Watson, H. C., *Prog. Stereochemistry*, **4**, 299 (1969).
- ⁷ Pauling, L., *Stanford Med. Bull.*, **6**, 215 (1948).
- ⁸ Griffiths, J. S., *Proc. Roy. Soc., A*, **235**, 23 (1956).
- ⁹ Ibers, J. A., and La Placa, S. J., *J. Amer. Chem. Soc.*, **87**, 2581 (1965).
- ¹⁰ Christoph, G. G., Marsh, R. E., and Schaeffer, W. P., *Inorg. Chem.*, **8**, 291 (1969).
- ¹¹ Wang, B.-C., and Schaefer, W. P., *Science*, **166**, 1404 (1969).
- ¹² Calligaris, M., Nardin, G., and Randaccio, L., *Chem. Commun.*, 763 (1969).
- ¹³ Caughey, W. S., Alben, J. O., and Beaudreau, C. A., in *Oxidases and Related Redox Systems* (edit. by King, T. E., Mason, M. S., and Morrison, M.), 97 (Wiley, London, 1964).
- ¹⁴ Perutz, M. F., *Nature*, **228**, 726 (1970).

- ¹⁵ Brink-Shoemaker, C., Cruickshank, D. W. J., Hodgkin, D. C., Kamper, M. J., and Pilling, D., *Proc. Roy. Soc., A*, **278**, 1 (1964).
- ¹⁶ Lenhart, P. G., *Proc. Roy. Soc., A*, **303**, 45 (1968).
- ¹⁷ Calligaris, M., Minichelli, D., Nardin, G., and Randaccio, L., *J. Chem. Soc. (A)*, 2411 (1970).
- ¹⁸ Prout, C. K., and Wiseman, T. J., *J. Chem. Soc.*, 497 (1964).
- ¹⁹ Lenhart, P. G., *Chem. Comm.*, 980 (1967).

Selective Effects of Cholera Toxin on the Adrenaline Responsive Component of Hepatic Adenyl Cyclase

THE role of adenyl cyclase in cholera enteropathy has been extensively documented¹. We describe here experiments with mouse liver adenyl cyclase which suggest a possible mechanism for the stimulatory effects of cholera toxin.

Female Swiss albino mice (20 g) were given 20 γ of purified² cholera toxin intraperitoneally and killed after 4 h. Livers were perfused *in situ* (portal vein) with ice-cold KCl/K-acetate (0.13/0.02 M) solution at pH 7.4, minced, homogenized and used for preparation of a washed membrane particle³. Adenyl cyclase was assayed using ⁸¹⁴C-ATP and descending thin-layer chromatography on PEI cellulose⁴.

The effects of intraperitoneal cholera toxin on hepatic adenyl cyclase activity are shown in Table 1. We emphasize four points: (1) activation of adrenaline responsive adenyl cyclase by adrenaline was not observed in the toxin treated liver; (2) basal activity (adenyl cyclase activity in the absence of added hormone) in the liver of the toxin treated animal was equal to the adrenaline stimulated activity plus the basal adenyl cyclase activity in the control animal; (3) there was no effect of cholera toxin on the stimulation of hepatic adenyl cyclase activity by glucagon; and (4) stimulatory effects of toxin and glucagon were additive as were the effects of adrenaline and glucagon.

Previous studies in this laboratory have provided evidence for two discrete adenyl cyclase systems in liver, with separate regulatory and catalytic moieties^{5,6}. These data contrast with studies in fat cells where, because of non-additivity of hormonal stimulation, it has been suggested that the enzymatic activity of a single catalytic moiety is subject to control by several different regulatory moieties each with discrete hormone specificities⁷. In liver, the effect we have observed with cholera toxin is selective, involving the adrenaline component of hepatic adenyl cyclase exclusively. The effect seems stable in that it is produced *in vivo* and is not reversed by those manipulations which are required for the preparation of the washed particle enzyme *in vitro*.

Cholera toxin seems to mimic the effects of adrenaline on hepatic adenyl cyclase producing a fully activated enzyme in the cholera toxin treated animal which is not further activated by adrenaline. The glucagon responsive cyclase from the same liver is unaffected by cholera toxin and exhibits a normal response to glucagon. The data support our findings of

Table 1 Effects of Cholera Toxin on Liver Adenyl Cyclase

Hormone	Adenyl cyclase activity Control	Toxin-treated
Basal (no added hormone)	6.3	34.6
Adrenaline	33.4	35.2
Glucagon	43.6	68.5
Adrenaline and glucagon	67.6	70.1

Assays were carried out for 3 min at 37° C and terminated by immersion in boiling water. The concentrations of hormones and reaction conditions are as previously described³. Injections of cholera toxin are described in the text. Adenyl cyclase activity is expressed as nmol of cyclic AMP/10 mg/10 min. Triplicate values agreed with 6% and the averages for six determinations are given. The differences in basal activity between the two groups was significant ($P < 0.02$).

discrete adenylyl cyclase systems in liver^{3,5,6} as the effects of cholera toxin are additive with those of glucagon as are the effects of adrenaline. This argues for discrete catalytic sites with specific glucagon or adrenaline regulatory moieties rather than the existence of combinations of regulatory moieties controlling a single catalytic site.

Our findings provide an explanation for the glycogenolytic effect of intravenous cholera toxin⁸ and suggest that intestinal epithelial adenylyl cyclase may exhibit regulation by catecholamines. The present data do not provide insight into the chemical nature of cholera toxin effects on adenylyl cyclase nor do they indicate whether cholera toxin is present in the plasma membrane as an essential component of the toxin-modified adrenaline-responsive adenylyl cyclase in the liver of treated animals.

This work was supported by the National Institute of Arthritis and Metabolic Diseases and the American Cancer Society. We thank Drs Nathaniel F. Pierce and Richard A. Finkelstein for their gift of purified choleragen.

RONNIE E. GORMAN
MARK W. BITENSKY

Department of Pathology,
Yale University School of Medicine,
New Haven, Connecticut 06510

Received July 16, 1971.

¹ Feld, M., *New England J. Med.*, **284**, 1137 (1971).

² Finkelstein, R. A., and LoSpalluto, J., *J. Infect. Dis.*, **121**, S63 (1970).

³ Bitensky, M. W., Russell, V., and Blanco, M., *Endocrinology*, **86**, 154 (1970).

⁴ Bitensky, M., Gorman, R., and Miller, W., *Proc. US Nat. Acad. Sci.*, **68**, 561 (1971).

⁵ Bitensky, M. W., Russell, V., and Robertson, W., *Biochem. Biophys. Res. Commun.*, **31**, 706 (1968).

⁶ Gorman, R. E., and Bitensky, M. W., *Endocrinology*, **87**, 1075 (1970).

⁷ Birnbaumer, L., and Rodbell, M., *J. Biol. Chem.*, **244**, 3477 (1969).

⁸ Graybill, J. R., Kaplan, M. M., and Pierce, N. F., *Clin. Res.*, **18**, 454 (1970).

Cerebrospinal Fluid Levels of MHPG in Affective Disorders

THE catecholamine hypothesis of affective disorders^{1,2}, which associates decreased functional catecholamines with depression, has been tested by measurement of noradrenaline (NA) in plasma or urine or the NA metabolites, normetanephrine and VMA in urine³⁻⁵. Probably only a small percentage of these compounds originate from the central nervous system⁶, and so it is not surprising that this has led to conflicting results.

Some evidence indicates that the principal metabolite of NA in the mammalian brain is 3-methoxy-4-hydroxy-phenylethylene glycol (MHPG)⁶⁻⁹, although this conclusion has been questioned¹⁰. Maas *et al.*⁶ estimate that about 25% of the MHPG found in urine derives from brain, and Gitlow *et al.*¹¹ in human studies obtained similar figures by more indirect methods. Maas *et al.*^{12,13} have reported decreased levels of MHPG in the urine of depressed patients in whom other NA metabolite levels were normal.

MHPG has been identified in human cerebrospinal fluid (CSF)¹⁴ and can be measured¹⁵. We have therefore used this procedure on manic and depressed patients.

All patients selected were housed on the metabolic research unit, Department of Psychiatry, New York University—Bellevue Hospital Center, and were participants in other ongoing investigations. Subjects were divided into three phases: a baseline (placebo) period of 1 week; 3 weeks of drug treatment, and a post-placebo period of 1 week. Throughout the different phases, clinical rating and laboratory assessments were carried out. For our investigation, 10 ml. spinal

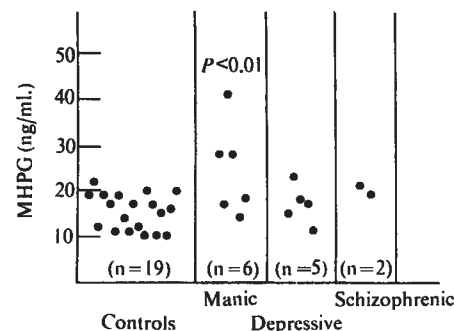


Fig. 1 Cerebrospinal fluid MHPG data comparison in thirteen hospitalized psychiatric patients and nineteen controls.

fluid was collected on the seventh day of baseline and also at the end of the 3 week period of medication, and immediately frozen. All psychiatric diagnoses were established by unanimous agreement among three psychiatrists and included the following groups: cyclic manic-depressive psychoses, manic-phase (6), schizophrenic reaction, schizo-affective type, excited (2), endogenous depression (bipolar (2), unipolar (2) and reactive depression (1).

Total MHPG (free + conjugated) was determined in duplicate on 2-ml. specimens of CSF¹⁵. Homovanillic acid (HVA) was measured by the method of Gerbode and Bowers¹⁶ and 5-hydroxyindoleacetic acid (5-HIAA) by the method of Ashcroft and Sharman¹⁷. Patients' metabolite levels were compared with values obtained from normal control subjects (19) most of whom were tapped for herniated disks.

The mean CSF levels of the dopamine metabolite HVA and the serotonin metabolite 5-HIAA in the patient groups were not significantly different (student *t* test unpaired data) from the mean normal levels (Table 1). The HVA levels of the depressed patients tended to be lower than normal levels. This has been attributed to decreased motor activity¹⁸, but this explanation is not valid here because two of the five depressed patients were agitated; the other three were apathetic, lethargic and dejected.

The five depressed patients studied all showed MHPG levels within the normal range (Fig. 1). The two schizo-affectives also showed normal MHPG levels; these schizophrenic subjects were selected because of their hyperactive behaviour and used as controls for motor activity. Three of the six manic patients has MHPG levels elevated beyond the normal range. For the manic group as a whole, the difference was significantly higher than the control patients ($P < 0.01$, student *t* test of unpaired data). Treatment of two manic patients with lithium carbonate resulted in a sharp drop in MHPG levels, a moderate increase in HVA and a sharp increase in 5-HIAA (Fig. 2). Both patients were no longer manic when the second tap was drawn. Two other manic patients showed no consistent metabolite changes after treatment with chlorpromazine; one subject was still manic at the end of the treatment period with MHPG levels still high after treatment; the second patient had normal MHPG levels at baseline and was extremely manic; he was depressed after therapy with no change in MHPG.

Treatment with different psychoactive drugs to the depressed and schizophrenic patients did not alter the normal MHPG

Table 1 Cerebrospinal Fluid Levels of HVA and 5-HIAA in Patients with Affective Disorders

		Normals (N=19)	Manic (N=6)	Depressive (N=5)
HVA * (ng/ml.)	Range	3-50	3-15	0-13
	Mean	$\bar{X}=18$	$\bar{X}=11$	$\bar{X}=7$
5-HIAA * (ng/ml.)	Range	15-55	12-38	16-63
	Mean	$\bar{X}=29$	$\bar{X}=22$	$\bar{X}=25$

* HVA was measured by the method of Gerbode and Bowers¹⁶, and 5-HIAA by the method of Ashcroft and Sharman¹⁷.

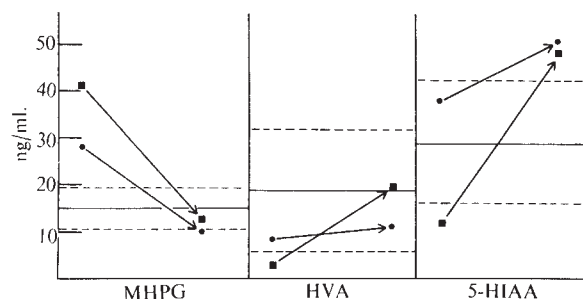


Fig. 2 Change in amine metabolites (MHPG · HVA · 5-HIAA) in two manic patients during treatment with lithium carbonate. —, Mean; --- s.d. for normals.

levels in spinal fluid irrespective of clinical outcome. We conclude that brain NA may not be lowered in depression, and that some manic patients may synthesize abnormal amounts of brain NA. The therapeutic effect of Li^+ may be due to interference in this process. It is not clear whether the high levels of MHPG represent a primary biochemical defect or secondary factors; but two agitated schizo-affective patients had normal levels of MHPG. Our preliminary results are consistent with the hypothesis¹⁹ that only the manic phase of manic depressive illness is associated with abnormal brain NA levels.

S. W. is supported by a Research Career Development award and US Public Health grant. B. S. and S. G. are supported by a US Public Health grant.

SHERWIN WILK

Department of Pharmacology,
Mount Sinai School of Medicine of the
City University of New York,
100th Street and Fifth Avenue,
New York, NY 10029

BARON SHOPSIN
SAMUEL GERSHON
MICHAEL SUHL

Department of Psychiatry and Neurology,
New York University Medical Center,
550 First Avenue,
New York, NY 10016

Received May 18; revised July 5, 1971.

- ¹ Bunney, jun., W. E., and Davis, T. M., *Arch. Gen. Psychiat.*, **13**, 483 (1965).
- ² Schildkraut, J. J., *Amer. J. Psychiat.*, **122**, 509 (1965).
- ³ Wyatt, R. J., Portnoy, B., Kupfer, D. J., Snyder, F., and Engleman, K., *Arch. Gen. Psychiat.*, **24**, 65 (1971).
- ⁴ Nelson, G. N., Masuda, M., and Holmes, T. H., *Psychosom. Med.*, **28**, 216 (1966).
- ⁵ Takahashi, R., Nagao, Y., Tsuchiya, K., Takamizawa, M., Kobayashi, T., Toru, M., Kobayashi, K., and Kariya, T. J., *Psychiat. Res.*, **6**, 185 (1968).
- ⁶ Maas, J. W., and Landis, D. H., *J. Pharmacol. Exp. Ther.*, **163**, 147 (1968).
- ⁷ Mannarino, E., Kirshner, N., and Nashold, B. S., *J. Neurochem.*, **10**, 373 (1963).
- ⁸ Rutledge, C. O., and Jonason, J., *J. Pharmacol. Exp. Ther.*, **157**, 493 (1967).
- ⁹ Schanberg, S. M., Schildkraut, J. J., Breese, G. R., and Kopin, I. J., *Biochem. Pharmacol.*, **17**, 247 (1968).
- ¹⁰ Chase, T. N., Breese, G. R., Gordon, E. K., and Kopin, I. J., *J. Neurochem.*, **18**, 135 (1971).
- ¹¹ Gitlow, S. E., Mendlowitz, M., Bertani, L. M., Wilk, S., and Wilk, E. K., *J. Clin. Invest.*, **50**, 859 (1971).
- ¹² Maas, J. W., Fawcett, J., and Dekirmenjian, H., *Arch. Gen. Psychiat.*, **19**, 129 (1968).
- ¹³ Maas, J. W., Dekirmenjian, H., and Fawcett, J., *Nature*, **230**, 330 (1971).
- ¹⁴ Schanberg, S. M., Breese, G. R., Schildkraut, J. J., Gordon, E. K., and Kopin, I. J., *Biochem. Pharmacol.*, **17**, 2006 (1968).
- ¹⁵ Wilk, S., Davis, K. L., and Thacker, S. B., *Anal. Biochem.*, **39**, 498 (1971).
- ¹⁶ Gerbode, F., and Bowers, jun., M. B., *J. Neurochem.*, **15**, 1053 (1968).
- ¹⁷ Ashcroft, G., and Sharman, D. F., *Brit. J. Pharmacol.*, **19**, 153 (1962).

- ¹⁸ van Praag, H., and Korf, J., *Psychopharmacologia*, **19**, 199 (1971).
- ¹⁹ Bunney, jun., W. E., Murphy, D. L., and Goodwin, F. K., *Lancet*, **i**, 1022 (1970).

Antibody-stimulated Increase in Sex Pili in R^+ Enterobacteria

ALTHOUGH a single bacterium may bear hundreds of common pili there are seldom more than two or three sex pili, corresponding roughly to the number of copies of the sex factor genome. This finding supports the suggestion that efficient transfer of F is due to the location of its genome near the mating substance on the cell surface¹, and fits with a more recent observation that transfer of a given sex factor only occurs in the presence of pili determined by its own genome². We report here a new observation, that the number of sex pili can be enormously increased simply by exposing metabolically active bacteria to antiserum to the sex pilus. These experiments show that there are fifty or more potential sites for pilus extrusion, not two or three as previously supposed.

The antigenic relationships of sex pili determined by F, F-like and I-like sex factors have been assessed by electron microscopical examination of the pili after addition of antiserum directly to the bacterial cultures³. In these conditions using live cultures carrying I-like sex factors, many more pili

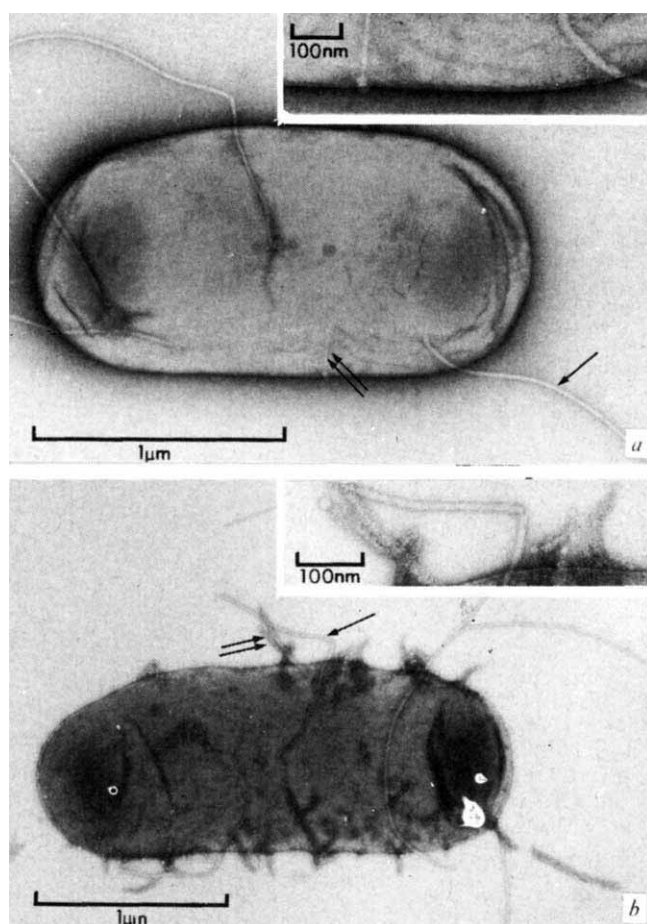


Fig. 1 Bacteria from a broth culture of *Escherichia coli* K12 strain 22(R538-2drd) freshly grown to a bacterial concentration of 10^8 ml^{-1} . a, Without specific antiserum. A double arrow marks the single sex pilus present; a single arrow marks a flagellum. The inset shows these structures enlarged; the sex pilus has a terminal knob. b, The same culture after mixing with specific anti-pilus serum at 37°C . One of the numerous antibody coated sex pili is marked by a double arrow; a single arrow marks a flagellum. The inset shows these structures enlarged; many of the pili have terminal knobs which are free of antibody³.

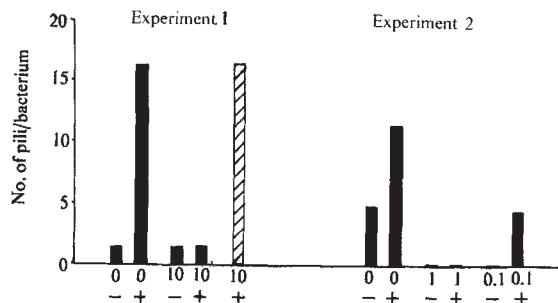


Fig. 2 Effect of formalin on serum-induced increase of sex pili. The height of each column represents the average number of pili per bacterium in a sample of strain 22(R538-2*drd*) grown in broth to a concentration of about 10^8 ml.⁻¹ and prepared for electron microscopy as in ref. 3. Either fifty or twenty-five bacteria were scored according to the numbers of pili present. Parallel samples were mixed with specific anti-pilus serum (columns marked +) or a serum not reacting with the pili (-) for 10 min at 37° C with or without previous exposure to formalin for 20 min at 37° C (percentage formalin indicated below column). The hatched column represents a sample treated with formalin after specific anti-pilus serum.

Fig. 3 Effect of temperature on serum-induced increase of sex pili. *A*, Drops of a broth culture of 22(538-2*drd*) grown to a bacterial concentration of 10^8 ml.⁻¹ and of either specific (+) anti-pilus serum or of a serum not reacting with the pili (-) were placed side-by-side in plastic Petri dishes floating on water at 11°, 15°, 20°, 25°, 37° and 52° C. After 20 min to reach the required temperature, the paired drops were mixed; 15 min later, samples were prepared for electron microscopy as described in ref. 3. The height of each column represents the average number of pili in a sample held at the temperature indicated below in °C. Either fifty or twenty-five bacteria were scored according to the numbers of pili present. *B*, Samples of another culture of 22(R538-2*drd*) and of another strain, 22(R64*drd*11), were similarly mixed with specific (+) or non-specific (-) antiserum. Samples held continuously for 30 min at 7° C (labelled 7) are compared with parallel samples held for successive 10 min intervals at 7°, 37° and 7° C (labelled 37) before final preparation at room temperature (20° C) for electron microscopy.

were observed when these had reacted with the antibody than when they remained uncoated. Nevertheless, unlabelled I-like pili are easily detected even when the image of the bacterium covers them (Fig. 1*a*). Fig. 1 illustrates the effect with bacteria carrying the de-repressed R factor R538-2*drd*. This ability of an antiserum to increase the numbers of sex pili was always associated with its ability to bind specifically to the type of pilus produced, even when absorbed sera were used which had a narrow specificity (typing sera distinguishing serotypes of the I-like class³). A trivial explanation would be that binding of antibody resulted in a greater retention of pili during the preparation of specimens for electron microscopy. The following experiments, using formalin or cold to arrest bacterial metabolism, establish that the increase is not due to this artefact but to an effect of antibody on pilus production.

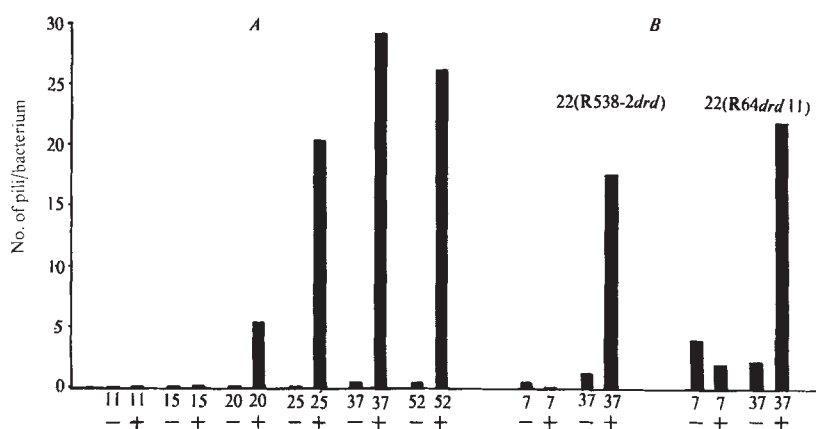
Added before antiserum, formalin abolished its effect (Fig. 2) without affecting antibody binding. However, an artefact was not entirely excluded because experiments with detached pili showed that formalin decreased their retention. The experiments using temperature variation illustrated in Fig. 3, and particularly that of Fig. 3*B*, in which a complex temperature sequence was used to ensure that preparation of cooled and warmed cultures was identical are not subject to this objection. These experiments show that the response to antiserum is abolished below a critical temperature of about 15° C although antibody binding to pili is unaffected at this temperature. No increase of pili occurred if the antiserum, added at below the critical temperature, was washed off before raising the culture to 37° C, nor was preheating to 37° C effective if the bacteria

were subsequently cooled to 10° C before adding antiserum. These tests showed that for an increase of pili to occur the bacteria must be at a temperature above 15° C while antibody is present.

The rate of pilus production was examined by making mixtures of bacteria and antiserum at 10° C and then transferring them to higher temperatures. Pili were produced so rapidly at 37° C that the maximum number were present in samples taken even at 1 min. At 20° C, the increase was slower: in 1 min, a few short pili were seen on 6% of the bacteria and an occasional bacterium had many pili; by 3, 6 and 12 min, progressively larger proportions had become abundantly pilated.

It has not so far been possible to show conclusively that antibody increases the numbers of F-like sex pili. This may be partly because there are, as a rule, more F-like than I-like pili before addition of antibody, and also because F-like sex pili tend to be longer and to form tangled skeins so that it is difficult to estimate their numbers.

The literature on production of sex pili deals chiefly with F pili, whose production has been shown to be temperature-dependent⁴, which are regenerated within a few minutes after



mechanical removal⁴⁻⁶ and which disappear with starvation⁷. There is no reason to suppose that production of I-like sex pili is fundamentally different, and it now appears that this can be influenced by a molecule which binds to the pilus and is generally assumed not to penetrate to the interior of the cell. Two kinds of explanation suggest themselves. If, as has been postulated⁸, sex pili are alternately extruded and retracted, the binding of antibody might prevent retraction and thus increase the numbers of pili in the extruded state. Alternatively, attachment of antibody might bring about extrusion by upsetting a normal equilibrium between free pilin molecules and polymerized pili at the assembly site.

A. M. LAWN
ELINOR MEYNELL

Departments of Electron Microscopy and Microbiology,
Lister Institute of Preventive Medicine,
Chelsea Bridge Road, London SW1

Received July 9, 1971.

- Jacob, F., Brenner, S., and Cuzin, F., *Cold Spring Harbor Symp. Quant. Biol.*, **28**, 329 (1963).
- Salzman, T. C., *Nature New Biology*, **230**, 278 (1971).
- Lawn, A. M., and Meynell, E., *J. Hyg., Camb.*, **68**, 683 (1970).
- Brinton, C. C., *Trans. NY Acad. Sci.*, **27**, 1003 (1965).
- Novotny, C., Carnahan, J., and Brinton, C. C., *J. Bact.*, **98**, 1294 (1969).
- Novotny, C., Raizen, E., Knight, W. S., and Brinton, C. C., *J. Bact.*, **98**, 1307 (1969).
- Curtiss, R., Caro, L. G., Allison, D. P., and Stallions, D. R., *J. Bact.*, **100**, 1091 (1969).
- Marvin, D. A., and Hohn, B., *Bact. Rev.*, **33**, 172 (1969).

BOOK REVIEWS

Mössbauer Compendium

Mössbauer Spectroscopy. By N. N. Greenwood and T. C. Gibb. Pp. xii + 659. (Chapman and Hall: London, October 1971.) £12.

THE phenomenal growth of the use of nuclear gamma ray resonance spectroscopy—more commonly referred to as the Mössbauer effect—in the solution of chemical problems has been paralleled by an equally phenomenal rate at which this field is reviewed, surveyed, summarized and systematized. The reasons for this state of affairs are not difficult to deduce: the Mössbauer effect has been used to elucidate problems in chemical structure, chemical bonding, magnetism, hot atom effects, nuclear lifetimes, nuclear decay schemes, surface effects such as corrosion and catalysis, the study of alloys, biologically significant molecules, organometallic compounds, and a wide range of other problems. Consequently the structural chemist, the synthetic chemist, the nuclear physicist, the metallurgist, the biologist, and all the other practitioners of specialized subfields in the physical and biological sciences have felt a need to survey Mössbauer spectroscopy for their peers and colleagues, and have felt—rightly or wrongly—that the application of this spectroscopy to their area of science merited an individualistic treatment.

While one may question the validity of this approach in some fields, there can be little question of its appropriateness in the area of inorganic and metal-organic chemistry and related fields. The range of chemical problems which have been studied by Mössbauer effect spectroscopy is so wide that a book written by chemists, primarily for chemists, when well done, can only be considered a welcome addition to the scientist's bookshelf. This volume clearly falls into that category.

Greenwood and Gibb preface the main body of their work with three chapters which cover the fundamental physics of the Mössbauer effect, experimental techniques and hyperfine interactions. While the coverage of these topics is not (and was not intended to be) exhaustive, it is more than sufficient

to serve as a basis for a clear understanding of what is to follow. Any limitation in the range and depth of the material discussed in the individual chapters is adequately dealt with in the references to the scientific literature given in the extensive bibliography at the end of each chapter. After the interlude of a very brief (7-page) survey of applications of the Mössbauer effect to such areas as relativity and general physics, nuclear physics and solid state physics and chemistry, the reader comes to what is obviously the real love of the authors: nine chapters on Mössbauer effect spectroscopy in the field of iron chemistry, followed by chapters on tin, main group elements (including important and extensive discussion of antimony, iodine and xenon), transition metal elements, rare-earth elements and the actinides. It is, however, in the 284 pages devoted to Mössbauer effect studies using the 14.4 keV gamma transition in ^{57}Fe that the authors' extensive knowledge of the field and critical judgment of subject matter come through most strongly. The exposition here is not only lucid and well organized, but most clearly reflects the special expertise of the authors in terms of the (sometimes conflicting) interpretations of results which have been offered in the scientific literature. In writings which deal with quantitative experimental results collected from a wide range of sources, it is useful and convenient to summarize such data in tabular form for convenient access by the reader. In this regard, the present volume is particularly useful since there are extensive collections of tables of data which summarize in a convenient and economical way much of the information most useful to the reader. In this context it is appropriate to note that the authors have quoted isomer shifts not only with respect to a common reference point (for example, SnO_2 for ^{119}Sn spectroscopy, metallic iron for ^{57}Fe , etc.) often arrived at by recalculating the original data, but have also preserved for the critical reader the numerical data cited by the original authors. The only regrettable omission in some of these data tables (see, for example, Table 9.4 on iron cyclopentadiene compounds or

Table 14.5 on tin (IV) halide derivatives) is the temperature at which the measurements were made.

The overall format of this volume meets appropriate standards, although some of the figures are badly reproduced from the originals, making them less useful than they might be. The author and subject indices are comprehensive and add considerably to the overall usefulness of the book, as do the detailed references at the end of the individual chapters. (The inclusion at the bottom of each page of text of the page numbers of the references for the chapter in question is especially convenient and constitutes a welcome practice.) On the other hand, the quality of the bookmaking (in the nonspeculative sense) leaves much to be desired. In a volume selling for £12, the purchaser has a right to expect a sturdy binding, a spine which survives casual usage, and figure reproductions which are free from smudges and poor inking of the plates. In all of these aspects the efforts of Chapman and Hall fall short of the standards which one can reasonably expect at that price.

In summary, then, this book is a most useful and usable addition to the literature on Mössbauer effect spectroscopy, written by two authors who have not only themselves made significant contributions to this field, but who are also competent to exercise critical judgments in evaluations of the results which have been published. Any chemist who is seriously interested in using Mössbauer effect spectroscopy in his field will find this book a welcome addition to his library. Certainly no working science library should fail to include it in its holdings. It is possible that this will be the last book with broad coverage (in terms of chemistry) on Mössbauer effect spectroscopy, for the field has become so large and diversified that comprehensive reviews of the totality of the work which has been done become unmanageable. If this turns out to be the case, *Mössbauer Spectroscopy* by Greenwood and Gibb serves as a fitting summary, after one decade, of the application of this technique to the solution of a wide range of chemical problems.

R. H. HERBER

Animals in Context

The Animal and the Environment. By F. John Vernberg and Winona B. Vernberg. Pp. xv + 398. (Holt, Rinehart and Winston: New York and London, 1970.)

SOMETHING outside the normal ecology text, this book focuses attention on the individual animal species and its interaction with the environment. The nature of a community inhabiting a given environment is dependent upon the individual species which comprise that community, and the authors point out that the understanding of the factors determining the distribution of individual species will therefore go a long way towards elucidating that complex entity, the ecosystem. While readers expecting something new on the pressing problem of pollution might well be disappointed, the general zoologist and teachers of university courses in comparative physiology and ecology should find this book of interest.

At a time when ecology tends more and more towards the mathematical and physiology concentrates on the cell, the Vernbergs draw attention to the value of whole animal experimental studies on the adaptations of animals to a particular habitat and niche. This is not to say that the population or cellular levels are ignored; in adopting an autecological approach the authors have merely regarded the animal as the basic unit. The first three chapters of the book serve to outline the approach. The organism is introduced as a dynamic metabolizing entity which has become adapted to continued existence and reproduction in a fluctuating environment, while the second chapter surveys the biosphere with particular attention to abiotic components which necessitate adaptations on the part of animals. Chapter 3 contains a discussion of the effects on animals of temperature, salinity, gases and desiccation, the environmental factors most likely to be lethal, and thus limiting, in animal distribution. The physiological effects of these components are discussed in introducing the concept of a zone of resistance often modifiable by acclimatization. Attention is also drawn to the possibility of different stages in the life cycle having different requirements, thus stressing the need to study the whole of an animal's biology if the factors limiting its distribution are to be determined. The authors are fully aware of the limitations of single factor experimental studies and touch both on the desirability of and the difficulties encountered in carrying out experimental studies on the interaction of multiple environmental factors.

A consideration of respiration and habitat follows in which the effects of environmental variables on the efficacy

of respiratory systems and adaptations for survival under particular environmental conditions are discussed. The emphasis is on adaptation to habitat and adaptability to environmental gradients within a habitat. Ion and water balance and the maintenance of a constant internal environment receive a similar treatment. A chapter on perception and the environment leads the account from the influence of abiotic to that of biotic factors. Habitat selection in response to the perception of abiotic environmental components gives way to a consideration of the importance of being able to perceive stimuli relating other organisms in the environment, be they food, predators or conspecifics. From here on, the book follows more or less conventional ecological lines, with chapters on energy relationships, population continuity, population regulation and animal associations. Throughout, however, the emphasis is on the effects of the previously discussed environmental factors.

The final two chapters deal with the complex situations found in ecosystems, bringing in the concepts of succession, trophic levels, productivity, energy flow and chemical cycling, stressing the delicate balance of these systems. The book concludes with a description of the upsetting of this balance by pollution and other means which result in the destruction of habitat.

The Animal and the Environment is well written, in a clear economical style. The examples chosen by the authors to illustrate the various principles are pertinent, graphs and tables of actual experimental results are used to good effect and the chapters follow logically, thus adding up to an eminently readable account. Each chapter is followed by a useful summary and by a comprehensive list of references. A shortcoming of the book might be its restriction of cited examples almost entirely to marine poikilotherms. It must be conceded, however, that in giving greater emphasis to the field in which they are most authoritative, the Vernbergs have been able to draw on firsthand knowledge which has no doubt contributed to the book's readability. In any event, since it sets out to illustrate principles rather than to review, the comparative neglect of other habitats cannot be regarded as serious. The authors are aware of this shortcoming, themselves drawing attention to it in the preface. The reader is guided to literature dealing with aspects not covered in the text.

The value of the Vernbergs' book lies in that it bridges the gap between the physiologist and ecologist. Attending a symposium on terrestrial animal ecology some years back I became acutely aware of this gap; physiological ecologists and population ecologists seemed most often

each to be almost completely ignorant of the other's approach. With this in mind, those responsible for university courses in ecology and in comparative animal physiology might profitably make use of this book to place their respective disciplines in perspective. While it cannot at this level replace standard texts in ecology and comparative physiology, it should certainly prove useful as an additional or subsidiary text. In addition, it is of general interest to zoologists, regardless of speciality, in that it places the living animal in its proper context.

J. HEEG

Huxley and Education

T. H. Huxley on Education. (A selection of his writings with an introductory essay and notes by Cyril Bibby.) Pp. xii + 228. (Cambridge University: London, November 1971.) £2.80.

DR BIBBY'S fourth book on Huxley, which forms one of the publisher's useful series of texts in the history of education, is dedicated to "all teachers who hate humbug and cant and are therefore also educators". Another scientist-educationalist, Henry Armstrong, who had heard the "bulldog" lecture, maintained that Huxley's educational reputation rested on his writings rather than on his personal teaching ability. Huxley was the acknowledged leader of the Victorian scientific movement, which sought a place for science in schools and a realistic approach to university and technical education, or the abolition of voluntarism and administrative nihilism, not merely because of the sparkle and thrust of his prose, but also because of his astonishing physical energy in committees, on commissions, and through private lobbying. "Education is the instruction of the intellect in the laws of Nature," he wrote in the superb essay on liberal education in 1868. Science had to become part of every man's education; but the laws of nature he had in mind were not simply those of the new journal *Nature*—laws of "things and their forces"—but also sociology, the laws of "men and their ways". In his Huxley Memorial Lecture in 1933, Armstrong argued that there was still an urgent need to "honour Huxley's will", for only the shadow of Huxley's conception had been executed in the curricula of schools and universities. Perhaps a start on its substance has been made at last in the universities of Edinburgh, Manchester and Sussex where students can gain an awareness of science as a social phenomenon.

Dr Bibby has selected from nearly twenty of Huxley's didactic, but immensely enjoyable, pedagogic essays,

and prefaced them by a long and elegant essay on Huxley's life and his influence on education. In addition, he provides a chronology, bibliography and index. The essays selected are timeless: quite apart from their historical importance, Huxley's ideas and ideals bear on many contemporary issues such as specialization in science education, the nature and role of technical and technological education, and the place of examinations. The essays deserve to be read again.

W. H. BROCK

British Geology

The History of British Geology. By John Challinor. Pp. 224. (David and Charles: Newton Abbot, November 1971.) £3.50.

THE title of this book is misleading, for it is not a *history* of British geology, but, as its sub-title suggests, a bibliographical guide to the principal contributions made to the advancement of geological knowledge in Great Britain. A more appropriate title might be "Source Book of British Geology". The period covered extends from about 1538, when John Leland made some interesting geological observations during his tour of Britain, right up to the present day, but the majority of papers listed are those published in the 19th and 20th centuries. The area covered includes England, Wales and Scotland, but excludes Ireland. This is regrettable, because, geologically speaking, Ireland cannot be dissociated from the rest of the British Isles, and there has been a mutual exchange of ideas between geologists working in Ireland and in Great Britain.

There are two main sections in the book. The first, entitled "Primary Literature", is a chronological list of references to important contributions to the progress of British geology. This section is restricted mainly to papers embodying original research, but it also lists some composite works such as Geological Survey memoirs and important textbooks.

The second and longer section is entitled "Major Themes". These number eighty-six in all, and each is discussed briefly. As would be expected, they too deal mainly with developments that have taken place in the 19th and 20th centuries. Cross references are made to the primary literature, and also to an additional list of references entitled "Secondary and Associated Literature", contained in Appendix A. The latter are mainly papers or books dealing either specifically or incidentally with the history of geology in Britain, together with some others bearing on the development of British geology in a more general way than those cited in the primary list.

Appendix B contains an index of authors cited, with, in some cases, short biographic details. Appendix C is an index of place names, stratigraphic divisions and fossils, with cross references to both the "Primary Literature" and the "Themes" in which they are mentioned.

The author states that his purpose is "to provide a short introduction to a great and hitherto entirely neglected subject, the general history of British geology", by reviewing some of the written records that mark the progress of the science in Britain. His conclusion that the subject has been neglected is certainly correct. There exists no systematic and detailed account of the progressive development of geology as a whole in this country, or even of any of the several subdivisions of the subject, that covers the whole of the last 140 years or so, the period following the publication of Lyell's *Principles of Geology*, during which many major advances have taken place.

This work is no more than its author claims, an introduction to the subject. His choice of sources is necessarily arbitrary. He makes no claim for finality or infallibility, and would, I am sure, willingly admit that others might make different choices, or that there may be important omissions. One might, for example, have expected mention of the fact that the long series of annual Presidential Addresses published by the Geological Society of London since 1828 provide a valuable source of information about the progress of British geology. It may be suggested, too, that a more systematic arrangement of the themes would be helpful to the reader. This is, however, a pioneer work, the first of its kind.

Although it can be supplemented by consulting the author's *Dictionary of Geology*, where other source references are to be found, as it stands it provides a valuable and welcome guide to the development of geology in Great Britain, and, it may be hoped, will stimulate further study of the subject.

V. A. EYLES

Mendel to Morphogenesis

Molecular Genetics: an Introductory Narrative. By Gunther S. Stent. Pp. 650. (W. H. Freeman: San Francisco, 1971.) £5.10.

Molecular Biology of the Gene. By James D. Watson. Pp. 662. (W. A. Benjamin: New York, 1971.) Hardback \$16.50; paperback \$10.95.

FROM their lists of contents, these two books seem to have much in common. Each starts with a chapter on classical Mendelian genetics, continues with a consideration of the chemistry of the cell and then proceeds to look in greater

depth at the mechanisms by which genes are expressed. Stent considers in some detail the processes by which genetic information is transferred between bacteria, and his discussion of transformation, conjugation and transduction gives his book a balance not dissimilar to that of Professor W. Hayes's book *The Genetics of Bacteria and their Viruses*. Stent comes last to the genetic code and the mechanisms and control of protein synthesis whereas Hayes takes these topics in the reverse order. Stent's book is an introduction, however, which does not aim to compete with the more advanced treatment to be found in Hayes.

Watson's book is, of course, a revised version of his very successful first edition. He progresses directly from the physico-chemistry of cells to the structure and function of DNA and then to the genetic code and protein synthesis, concluding with chapters on what might be termed the future growth points of molecular biology—embryology at the molecular level, antibody synthesis and the problem of the cancer cell. Stent concludes with a single chapter, "Ramifications", in which he discusses the implications for cell biology of molecular biology and deals with problems similar to those discussed by Watson. The two books are written at comparable levels, with Stent's perhaps the more detailed, and each is adequately indexed.

But in spite of these superficial similarities, the two books embody different approaches to molecular biology. Stent's view is in the terms of genetics; Watson's approach is more physico-chemical. Whereas Stent's more historical treatment gives what is perhaps a better understanding of how the subject developed and why critical experiments were performed, Watson's approach yields a clear view of molecular biology more as a discipline in its own right, less an offshoot—albeit a distinct one—of genetics.

It goes without saying that both books are well written and each fulfils its aims well. It would be invidious to make any recommendation to distinguish between them. But for those students whose interests lie more in the work which has been performed with bacteria, including those genetic systems peculiar to microorganisms, Stent's book has an evident appeal; his historical approach is executed with great success. For those students more interested in what might be termed the story of how DNA makes RNA makes protein, told like it is, Watson's book will be the handier. Each book offers a valid perspective from which to view molecular biology; the only safe recommendation to aspiring molecular biologists is to read both of them.

BENJAMIN LEWIN

Flashing Lights

The Perception and Application of Flashing Lights. (International Symposium held at Imperial College, London, under the joint auspices of the National Illumination Committee of Britain and the Applied Optics Section, Imperial College, April 1971.) Pp. x+429. (Adam Hilger: London, September 1971.) £7.

THE use of flashing lights to attract attention and transmit information is now very widespread, especially during travel by sea, land, or air, and is undoubtedly a matter of considerable practical importance. The primary objective of this symposium was to bring together the scientists and engineers concerned with the design of flashing light signals with those who use such signals, and with those engaged in studies of perception. Participants at the symposium thus came from a wide variety of disciplines, and the meeting was divided into six sessions, dealing with the visual perception of flashing lights, general, marine, road and rail, and aviation applications, and future research possibilities.

The result is an intriguing juxtaposition of theoretical and practical articles, but with little cross-talk between the two. At the practical level, for example, we are given details of the electrical circuits used in the flasher indicators of cars, the mechanical construction of occulting hood lighthouse lamps, and the design of anti-collision lights for aircraft. This practical approach is also well exemplified by a paper devoted to the perception of short flashes, one purpose of which was to see whether the length of the flashes given out by US Coastguard battery-powered buoys could be reduced by a third, with a consequent saving of \$500,000 each year. Interspersed with such papers are contributions on visual perception quite unconnected with any application. Thus there are papers dealing with the Bezold-Brücke phenomenon and theoretical models of the absolute threshold, and there is a contribution (for some reason appearing in the middle of the session on road and rail applications) which describes a theoretical model of the visual system to account for the perception of apparent motion.

The lack of standardization of flashing signals comes out very clearly in this symposium. The standards specified for motor vehicle lights differ between European countries, and even more widely between them and the USA, and there is still less standardization of airport lights. This is particularly important for aircraft, which pass rapidly from country to country, and apparently a pilot's first problem on seeing a light from the air is not to get information from it, but

to decide which system it forms part of. Economics come into this also, and at one point it is suggested that the air industry cannot afford not to improve its safety record because the cost (in money) of accidents is now too high: deaths appear to be a secondary consideration! The general impression from many of the chapters is of a world filling up with more and more flashing lights, each one made stronger than its predecessors in an effort to make it stand out from the visual chaos that forms its background.

Theoretical concepts and studies seem to have made disappointingly little contribution to the solution of these practical problems, most of which have been studied empirically. This is probably partly due to the unrealistic situations used in the laboratory, where attention is commonly controlled by fixation lights and visual thresholds are usually measured. In practical situations, however, the lights are often well above threshold, and attracting attention is a major problem. If this symposium does indeed lead to more contact between engineering and the academic study of perception it will have fulfilled a valuable function.

W. R. A. MUNTZ

Radiation Physics

Atomic and Molecular Radiation Physics. (Wiley Monographs on Chemical Physics.) By L. G. Christophorou. Pp. x+625 (Wiley Interscience: London and New York, July 1971.) £10.50.

THE study of the interaction of low energy particles and radiation with atoms and molecules has been a field of intense activity in recent years, largely as a result of the development of new and elegant experimental techniques which depend on sophisticated instrumentation, including high resolution electron spectrometry, phase sensitive detection, microwave methods and so on. The measurement of the cross-sections of the many processes of interest has been extended down to particle energies of a few electron volts or less and a remarkable and previously unsuspected series of resonances involving the formation of short-lived compound states has been revealed. Indeed, low energy electron collision physics has been to some extent dominated by the study of this resonance formation in a surprisingly analogous way to elementary particle physics at energies 10^8 times as great.

Recent work in the interaction of electrons and photons with atoms and molecules is reviewed in this monograph. Most of the book is concerned with interactions of electrons or photons of energies less than some hun-

dreds of electron volts but the first chapter deals with the processes involved in the interaction with matter of electromagnetic radiation of much higher energy and the rate of energy loss of energetic charged particles. This is followed by a detailed account of the interesting work on the measurement of the mean energy required to produce an ion pair by charged particles in matter, where in some cases the values obtained are markedly affected by very small impurities in the medium as a result of secondary ionization due to collisions of the second kind between excited atoms and impurity atoms of lower ionization potential. After an account of recent work on the interaction of photons with atoms and molecules, two long chapters are devoted to elastic and inelastic electron scattering processes. The chapter on elastic scattering deals at considerable length with results obtained using swarm methods most appropriate for electrons of very low energy. Beam methods are discussed comparatively less fully.

Subsequent chapters discuss at length the processes of negative ion formation and the measurement of detachment cross sections from negative ions and of electron affinities. The interactions of neutral and heavy charged particles—a field in which there is at least as much activity as in electron interactions—are dismissed in a few pages.

The book contains a very useful description of modern experimental methods in the field and collects together a great deal of data on cross sections, critical potentials, electron affinities, etc. The theoretical description is rudimentary and sketchy although the basic physical processes involved are discussed clearly. The discussion is not limited to the simplest atomic systems. Data on quite complicated molecular systems where the interpretation is much less certain are given and discussed. This is in line with the interest in the study of the interactions of electrons and photons with polyatomic systems in view of their likely importance in basic problems of life science. A short final chapter is indeed devoted to problems of biophysics and bioelectronics; unfortunately the expectation raised by the section headings is not matched by the information contained in the text. This will, however, undoubtedly become a field of great significance in the future and even by including such a brief chapter the author may kindle interest in the subject.

Altogether this represents a competent review of the present position in many aspects of the field and should prove a most useful reference book for the postgraduate student and research worker for whom it is intended.

E. H. S. BURHOP

CORRESPONDENCE

Overpopulation

SIR,—It may be true that neither this country nor the whole western world will be overcrowded in the foreseeable future. It may also be true that further efforts to reduce the birth rate might (if this country were a closed system) have serious economic consequences. But we are surrounded by an overpopulated and impoverished world. One service the wealthy nations could perform for that world would be to reduce their birth rates and make up the difference by immigration. Evidence from many countries suggests that a substantial reduction in birth rate to below replacement level can be achieved simply by making all methods of control freely available. Thus without any restrictive legislation and at negligible cost to ourselves, we could make a significant contribution towards stabilizing the world's population. The direct effect would be multiplied by the removal of young people to environments which would tend to lower their own fecundity, and by making our support of birth control in the underdeveloped parts of the world look more genuine.

Yours faithfully,

R. H. PRITCHARD

*Department of Genetics,
Adrian Building,
University Road,
Leicester LE1 7RH*

Publication Speed

SIR,—I was very interested to read Mr Griffiths's letter (*Nature*, 234, 425; 1971) on the speed and efficiency of the processing of articles submitted to learned and technical journals. I would be the very first to agree that the refereeing procedures for many learned and technical journals can be speeded up, and the examples quoted in the letter indicate a lack of efficiency in some quarters. However, the letter does indicate a failing common to many authors of "wanting to have their cake and eat it".

Quality journals have to maintain a stringent refereeing procedure. The task of reading and judging a high-class technical paper of, say, 8,000 words is no mean task. One must also bear in mind that referees are doing this work often in their spare time and are, in the majority of cases, receiving no fee. When one also takes into account that individuals in some much-researched fields receive numerous papers for adjudication from various separate journals, it is not difficult to see how delays occur.

It is, in my experience, a fact that many papers that "go wrong" in the course of refereeing do so because the author has not taken sufficient care in preparation and presentation. I would commend authors first to read carefully the guide to authors for a particular journal, and to ensure that the paper submitted follows the requirements in such matters as relevance of subject-matter, length, number of copies required, form of illustrations and so on. The requirements will have been included for a good reason, and often in the interest of ensuring speed of publication. I would emphasize the question of relevance of subject-matter, since this has been particularly commented on in Mr Griffiths's letter. In these days of high specialization, it is not always apparent to the editor that a paper is outside the subject field of his journal, and it may need a specialist referee to point this out. Particular examples of this occur in highly mathematical treatises.

Secondly, authors should take steps to obtain advice from colleagues, as to whether the paper would be likely to be accepted by the journal concerned. Too many authors seem prepared to send in a badly prepared paper as a "trial run". Such papers obviously waste a lot of referees' time and are generally more time-consuming to look through and assess than a well prepared paper.

I must register a strong reaction to the suggestion that authors might indulge in submitting a paper to more than one journal at a time. Apart from being contrary to the publication rules of most learned and technical journals, this again means that more referees are tied up in assessing papers. This is quite separate from the fact that two or more journals could simultaneously accept the paper, and possibly start a long and protracted copyright wrangle among themselves before it could be published.

Finally, an author who particularly requires speedy publication would be well advised to submit a short letter on the subject to one of the "Letters" journals in order to get his work "on the record" and then to follow this up with a carefully prepared full-length paper submitted to a journal relevant to the subject-matter of the paper.

Yours faithfully,

J. D. ST AUBYN

*Institution of Electrical Engineers,
PO Box 8,
Southgate House,
Stevenage, Herts SG1 1HQ*

First Biophysicist

SIR,—In his recent article "When does Information become Knowledge?" (*Nature*, 235, 86; 1972) Dr Wyatt commences with the comment "It is generally accepted that biophysics began with Avery". I find it surprising that such a subjective opinion should have been allowed to intrude in an otherwise objective paper. The accolade of being the first biophysicist has been popularly bestowed on all manner of individuals from Baron von Frankenstein to Francis Crick. In this department, however, we have our own prejudice on the matter. Perhaps a prophet is indeed not without honour except in his own country (or even in his own country, it would appear).

Yours faithfully,

JOHN E. LYDON

*Astbury Department of Biophysics,
University of Leeds, Leeds LS2 9JT*

Research Contracts

SIR,—I have been following with interest the recent proposals to alter the present system of science in Britain. Having experienced the present system in the United States at NASA and two medical institutions, I have observed the following situations, when science is contracted out.

(1) Much expensive duplication by rival competitors occurs. (2) Responsibility for the end product becomes indistinct when several contractors are involved in a single undertaking. (3) Many scientists carry out their own basic research clandestinely whilst on contract to provide a single service. (4) Technicians at a lower level in the contract system become less efficient because of the monotonous performance of a single task whose end result they never witness. (5) There is a general tendency to underemployment of individual capabilities of most of the scientists involved.

The contract system works for a specific technological task in which the basic research has already been established. However, as a national philosophy of science, the contract system leads to an unstructured bureaucracy and an uncontrolled military-industrial complex. Before changing the system it is necessary to establish a national priority list of scientific aims.

Yours faithfully,

BARBARA WOOD

*M.D. Anderson Hospital and Tumor Institute,
University of Texas, Houston*

Announcements

Miscellaneous

Professor G. Bernardini, Professor P. A. M. Dirac, Sir Nevill Mott, Mr J. A. Ratcliffe and Sir James Taylor have been elected honorary fellows of the **Institute of Physics**. The council of the Institute has made the following awards for 1972: Guthrie medal and prize, to **Dr B. D. Josephson**, University of Cambridge; Rutherford medal and prize, to **Professor A. Bohr**, University of Copenhagen; Glazebrook medal and prize, to **Sir Gordon Sutherland**, Emmanuel College, Cambridge; Maxwell medal and prize, to **Dr V. Heine**, University of Cambridge; Charles Vernon Boys prize, to **Professor M. W. Thompson**, University of Sussex; A. B. Wood medal and prize, to **Dr B. Ray**, Kingston upon Thames Polytechnic.

Erratum

In the article "Rods Cancel Cones in Flicker" by Donald I. A. MacLeod (*Nature*, 235, 173; 1972), the vertical axis of Fig. 1 should be labelled "Test patch intensity" and the horizontal axis "Background intensity"; in the legend to Fig. 1, the frequency symbolized by open triangles should read 4.5 Hz.

International Meetings

March 9, **New Aspects of Mechanism and Synthesis in Organic Systems**, London (The Chemical Society, Burlington House, London W1V 0BN).

March 11, **The Nervous System**, London (Miss M. J. Sellers, 2 Bramley Mansions, Berrylands Road, Surbiton, Surrey).

April 9-11, **Applications of Biomedical Technology**, Oxford (Mrs P. Ducker, Executive Secretary, Symposium on Biomedical Technology, Pergamon Press

Limited, Headington Hill Hall, Oxford OX3 0BW).

April 11-13, **Industrial Measurement and Control by Radiation Techniques**, Guildford (The Manager, Conference Department, Institution of Electrical Engineers, Savoy Place, London WC2R 0BL).

April 17-20, **Geochemical Exploration**, London (The Secretary, Institution of Mining and Metallurgy, 44 Portland Place, London W1N 4BR).

April 18-20, **Trends in On-line Computer Control Systems**, Sheffield (Manager, Conference Department, IEE, Savoy Place, London WC2R 0BL).

April 19-21, **Atmospheric Pollution**, London (Professor M. W. Thring, Mechanical Engineering Department, Queen Mary College, Mile End Road, London E1).

April 19-21, **Mechanical Aspects of Electronic Design**, Budapest (Conference Secretariat, Híradástechnikai Tudományos Egyesület Titkársága, Budapest V, Szabadság ter 17, Hungary).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Hooker's *Icones Plantarum*, Fifth Series. Vol. VII, Part IV: New or Noteworthy Species from Socotra and Abd al Kuri. Edited by Sir George Taylor, FRS. (Kew, Richmond: Benthams-Moxon Trustees, Royal Botanic Gardens, 1971.) £2. [1012]
The Natural Environment Research Council. Publications, Series C, No. 5: A Review of Recent Investigations of the Sea Bed on the Continental Margin Around the British Isles. Pp. 28. (London: The Natural Environment Research Council, 1971.) [1012]
Department of Trade and Industry. Technology and the Environment—Report from Scientific Counsellors. Pp. 30. (London: Overseas Technical Information Unit, 1971.) [1012]
Awards for Commonwealth University Staff, 1972-74. Pp. 102. (London: The Association of Commonwealth Universities, 1971.) 60p. [1012]
Wildfowl 22. Pp. 160+16 plates. (Slimbridge: The Wildfowl Trust, 1971.) £1.25: \$3.40. [1012]
The Leverhulme Trust—Seventh Report, 1968-1970. Pp. 107. (London: The Leverhulme Trust, 1971.) [1012]
Standing Commission on Museums and Galleries. The Preservation of Technological Material—Report and Recommendations. Pp. v+47. (London: HMSO, 1971.) 364p net. [1312]
Philosophical Transactions of the Royal Society of London. B: Biological Sciences. Vol. 263, No. 849 (9 December 1971): The Holonematidae

(Placoderm Fishes), a Review Based on New Specimens of *Holonema* from the Upper Devonian of Western Australia. By R. S. Miles. Pp. 101-234+ plates 16-23. (London: The Royal Society, 1971.) £4.20; \$10.90. [1312]
Greater London Council. Annual Report of the Scientific Adviser 1970. Pp. 110+9 photographs. (London: Greater London Council, 1971.) £1.20. [1512]
The University of Hull. Annual Report 1970/1971. Pp. 169. (Hull, The University, 1971.) [1512]
Agricultural Research Council. Annual Report of the Meat Research Institute, 1970/1971. Pp. 105. (London: Agricultural Research Council, 1971. Obtainable from HMSO.) £1 net. [1512]
Department of Employment. People and Jobs: a Modern Employment Service. Pp. 28. (London: Department of Employment, 1971.) [1512]
New Protein Foods. (A report of a Conference organized by the Agricultural Development Association in conjunction with the Department of Agriculture and Food Science, University of Reading.) Pp. 90. (York: Agricultural Development Association, 1971.) £1. [1512]

Other Countries

Organization for Economic Co-operation and Development. Review of National Scientific and Technical Information Policy—Canada. Pp. 162. (Paris: OECD; London: HMSO, 1971.) 11 francs; 85p; \$2.50. [612]
Canada: Department of Mines and Technical Surveys. Bulletin 197: Contributions to Canadian Paleontology (nine papers). By B. S. Norford *et al.* Pp. 133 (22 plates). \$6. Bulletin 201: Archaeocyatha from the Mackenzie and Cassiar Mountains, Northwest Territories, Yukon Territory and British Columbia. By Robert C. Handfield. Pp. 119 (16 plates). \$2. Bulletin 205: Comparative Study of the Castle River and other Folds in the Eastern Cordillera of Canada. By D. K. Norris. Pp. 58 (8 plates). \$2. Paper 70-10: Subsurface Cambrian Stratigraphy in Southern and Central Alberta. By D. C. Fugh. Pp. vi+33. \$5. (Ottawa: Information Canada, 1971.) [612]
Stadler Genetics Symposia, Vol. 3. Edited by Gordon Kimber and G. P. Rédei. Pp. 116. (Columbia, Missouri: University of Missouri, Agriculture Experiment Station, 1971.) \$4. [712]
Wattle Research Institute (South African Wattle Growers' Union; South African Timber Growers' Association, University of Natal; State Department of Forestry)—Report for 1970-71 (Twenty-fourth Year). Pp. 58. (Pietermaritzburg: Wattle Research Institute, University of Natal, 1971.) [812]
Comptes Rendus des Travaux du Laboratoire Carlsberg. Vol. 38, No. 11: Modification of Papain by Treatment with Glutaraldehyde Under Reducing and Non-Reducing Conditions. By Martin Ottesen and B. Svensson. Pp. 171-186. Vol. 38, No. 12: Ion Exchange Properties of the Glycocalyx of the Amoeba *Chaos chaos* and Its Relation to Pinocytosis. By K. B. Hendil. Pp. 187-212. Vol. 38, No. 14: Hydrogen Isotope Exchange in the Study of Protein Conformation: a Quantitative Test of an Exchange Mechanism. By Lars Willumsen. Pp. 223-296. Vol. 38, No. 15: Degradation of Endocytosed Albumin by *Chaos chaos*. By Y. S. Brownstone and C. Chapman-Andersen. Pp. 297-314. Vol. 38, Nos. 16-17: The Buoyant Titration of Native and Carbamylated Ovalbumin. By James B. Ifft. The Potentiometric Titration of Native Ovalbumin in Concentrated CsCl Solutions. By James B. Ifft and Lawrence G. Lum. Pp. 315-350. Vol. 38, No. 18: Synchronization of Cell Divisions in the Fission Yeast *Schizosaccharomyces pombe*, Using Heat Shocks. By B. Kramhoft and E. Zeuthen. Pp. 351-368. (Copenhagen: Danish Science Press, Ltd., 1971.) 11.50 D.kr each part. [912]

HOW TO BUY NATURE

Volumes start in January, March, May, July, September and November, but subscriptions may begin at any time.

The direct postal price per subscription is:

12 MONTHS* (52 issues per title)

	Surface mail UK and worldwide	U.S.A. and Canada
Nature (Friday)	£14	\$48
Nature + Nature Physical Science	£24	\$83
Nature + Nature New Biology	£24	\$83
All three editions	£29.50	\$108
Annual Index	£1	\$3

*Rates for shorter periods *pro rata* (minimum three months)
(Charge for delivery by air mail on application)

Editorial and Publishing Offices of NATURE

MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Number : 01-836 6833. Telegrams : Phusis London WC2R 3LF
Telex 262024

711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004
Telephone Number : 202-737 2355. Telex 64280

Subscription Department
MACMILLAN JOURNALS LIMITED
BRUNEL ROAD, BASINGSTOKE, HANTS
Telephone Number : Basingstoke 29242

American display advertisements
NATURE SCIENTIFIC PUBLICATIONS INC
711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004

All other advertisements
T. G. SCOTT & SON, LIMITED
1 CLEMENT'S INN, LONDON WC2A 2ED
Telephone : 01-242 6264/01-405 4743
Telegrams : Textualist London WC2A 2ED

Registered as a newspaper at the Post Office

Copyright © Macmillan Journals Limited, February 25 1972